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RACEMIZATION AND SOLVOLYSIS
of
MONO AND DIARYL SULFONIUM IONS

by

© CHRIS SCOTT

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE

OF M.Sc.

DEPARTMENT OF CHEMISTRY

EDMONTON, ALBERTA

FALL 1973

THE UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled "Racemization and Solvolysis of Mono and Diaryl Sulfonium Ions" submitted by Chris Scott in partial fulfilment of the requirements for the degree of Master of Science.

Supervisor

Date Fall 1973

ABSTRACT

The racemization and solvolyses of a number of optically active monoaryl and diaryl sulfonium salts have been investigated. The rate constants for racemization of these salts are compared with one another and with the rate constants for racemization of isopropylethylmethyl and cyclohexylethylmethylsulfonium perchlorates. The data provide information on both electronic and steric effects upon the racemization reaction.

Two features are clear from the data. Firstly, aryl groups do not have an appreciable electronic effect upon the rate of racemization of sulfonium salts. In the phenylethylmethylsulfonium system, introduction of a p-methoxy, p-hydroxy, or p-nitro group onto the phenyl group leads to an increase in the rate of racemization of less than a factor of 2. Both electron withdrawing and electron donating groups increase the rate of racemization by small amounts. This is good evidence for a racemization mechanism involving pyramidal inversion around the central sulfur atom. In the presence of one equivalent of sodium methoxide in methanol, p-hydroxyphenylethylmethylsulfonium perchlorate is converted to the corresponding zwitterion (p-O^-), and this compound racemizes only 4.3X faster than the unsubstituted compound. This again confirms that any electronic effect associated with substitution on the aromatic ring is very small. However, some resonance interaction via p-dπ

bonding between the positive sulfur and the adjacent carbon atom of the ring, leading to a barrier decrease in the activation energy for inversion, cannot be discounted.

The second clear feature from our data is that there is a marked steric effect upon the racemization rate. Replacement of the ethyl group in the phenylethylmethyl system by a p-anisyl group leads to an increase in the magnitude of k_{rac} by a factor of ca. 10 at 50°. Replacement of the methyl group in the phenylethylmethyl system by a p-anisyl group leads to an increase in the magnitude of k_{rac} by a factor of ca. 10^2 at 50°. Similarly, replacement of the methyl group in the phenylethylmethyl system by a larger primary group (n-propyl or n-butyl), leads to an increase in the magnitude of k_{rac} by a factor of ca. 10 at 50°. This latter result is somewhat surprising, however it is difficult to explain other than on steric grounds. These data provide the first good evidence for steric effects upon the inversion of acyclic pyramidal systems. A comparison of the rates of racemization for the phenylethylmethyl, isopropylethylmethyl and cyclohexylethylmethyl systems, where the steric effects should be similar, shows that the rate constants for racemization of these salts differ by less than a factor of 3.

Attempts to prepare optically active triaryl sulfonium salts were unsuccessful. However, making the assumption that steric effects will be additive in log k_{rac}, then from our data we can estimate the rate constant for racemization at 25° for the triaryl salt system.

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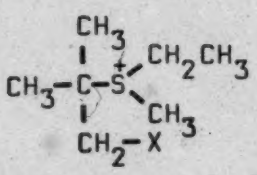
INTRODUCTION

Although optically active sulfonium salts were first prepared in 1900 (1,2), and the first mechanistic studies reported in 1930 (3), it was not until 1966 that the first evidence for the inversion of sulfur in sulfonium ions was reported. Darwish and Tourigny (4), found that t-butylethylmethylsulfonium salts racemized more rapidly than they decomposed. At 50°, in anhydrous methanol, the polarimetric rate constant, k_α, was found to be about 10X larger than the titrimetric rate constant, k_t. A similar behaviour was found in other solvents. In order to determine the mechanism which could account for the major path of racemization, a hydrogen in the t-butyl group was substituted by an electron withdrawing or electron donating group. The four compounds studied are shown below:



ClO_4^-

I, X=H

II, $X=OCH_3$

III, $X=CH_3$

IV, $X=C_6H_5$

The relative rates of ethanolysis at 50° of compounds: I : II : III : IV, were 1 : 0.06 : 6.3 : 1.1; and the relative rates of racemization in ethanol at 50° were 1 : 1.7 : 3.8 : 4.7.

In the solvolysis reaction, electron donating groups accelerated the reaction rate and electron withdrawing groups slowed the reaction rate. This is consistent with a mechanism involving heterolytic cleavage of the carbon-sulfur bond. This cleavage would result in formation of an ion - neutral molecule pair as shown in Figure I.

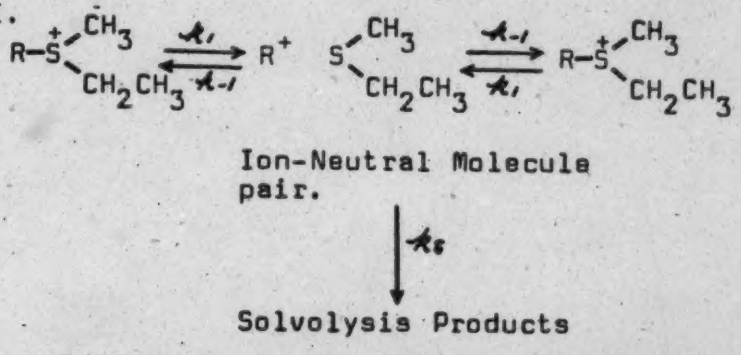


Figure I. Sulfur-alkyl bond cleavage mechanism for racemization and solvolysis.

The ion-neutral molecule pair can return to give racemic starting material, or react with the solvent to give solvolysis products. If the major pathway for racemization was via this mechanism, then electronic effects would be expected to affect the rates. However, substitution accelerates the rate of racemization whether the substituent is electron donating or withdrawing. This observation indicates that the major pathway for racemization involves a pyramidal inversion mechanism, which is not influenced by the electronic effect of the substituents, but is influenced by steric effects. Introduction of bulkier groups into the 1-position of the t-butyl group, increases the non-bonded interactions in the ground state, which can be relieved in the planar

transition state for inversion, Figure II.

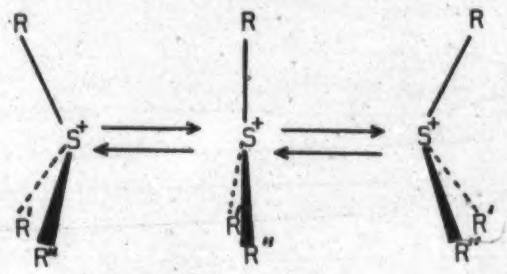
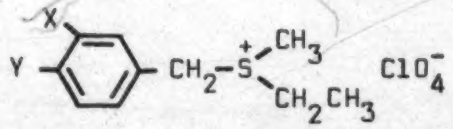


Figure II. Diagrammatic representation of inversion of $\overset{+}{S}R_3$

Darwish and Hui (5), have made a study of the benzylethylmethylsulfonium system. The following compounds were studied:



V, X=H, Y=H

VI, X=H, Y=NO_2

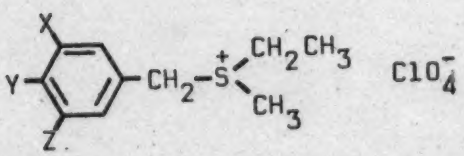
VII, X=NO_2, Y=OCH_3

VIII, X=H, Y=OCH_3

They studied the effect of such substitution on the rates of solvolysis and racemization, and showed that the major portion of the racemization for compounds V, VI and VII, could be accounted for by a pyramidal inversion about the central sulfur atom. Electron withdrawing and electron donating groups were found not to affect the rate of racemization significantly. At 50°, in anhydrous methanol, all three compounds racemized with a rate constant ($k_{rac}=k_{\alpha}-k_t$) of about 6×10^{-6} sec^{-1}. Under the same conditions, the relative rates of solvolysis of V : VI were 1 : 0.2. At 90°, the relative rates of methanolysis of V : VII were 1 : 0.65, showing a significant electronic effect on the solvolysis reaction. Compound VIII was found to exhibit behaviour markedly different from that of V, VI and VII. This compound underwent

solvolysis over 10^3X faster than V, in solvent methanol at 50^o, Also, k_{rac}, for compound VIII was found to be about 15X faster than k_{rac} for compound V. Since racemization by inversion was found not to be influenced by electronic effects, the accelerative effect of the p-methoxy group could not be explained by this mechanism. It was suggested that the major pathway for racemization was a carbon-sulfur bond heterolytic cleavage mechanism, already outlined in Figure I. This scheme accounted for the acceleration of both the solvolysis and racemization rates. This would seem to be a reasonable process, since the highly stabilized p-methoxybenzyl cation would be formed on bond heterolysis.

Further insight into the two pathways for racemization in the benzyl system was obtained by Darwish and Po (6), in which the solvolyses and racemization of various substituted benzylethylmethylsulfonium salts were investigated. The following compounds were studied:



IX, $X=NO_2$, Y=H, Z=H

X, $X=CH_3$, $Y=OCH_3$, Z=H

XI, $X=CH_3$, $Y=OCH_3$, $Z=CH_3$

XII, X=H, Y=Cl, Z=H

XIII, X=H, $Y=CH_3$, Z=H

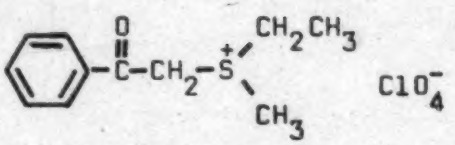
The relative rates of racemization in anhydrous methanol at 50^o of V : IX : X : XI : XII : XIII were: 1 : 0.96 : 48.2 : 1.79 : 0.95 : 0.99. The relative rates of solvolysis under the same conditions were: 1 : 0.36 : 3840 : 63.5 : 0.75 : 3.25.

The racemization rate constants for compounds IX, XII and XIII were found to be very close to that of the unsubstituted compound. In these cases, the electronic effects of the substituents did not influence the racemization rate significantly. This is consistent with a pyramidal inversion about the sulfur atom, serving as a major pathway to racemization. This mechanism also explains the excess of polarimetric rate constants, k_α, over the titrimetric rate constants, k_t. For example, compound IX was found to have a ratio of $\frac{k_\alpha}{k_t}=90$.

Darwish and Hui (5), had earlier suggested that compound VIII racemized predominately via a process other than pyramidal inversion, but by way of an ion - neutral molecule species (Figure I). In the study by Darwish and Po (6), it was concluded that compound X also racemized predominately by way of this latter mechanism. Support was given to this by a study of compound XI. In this case the racemization and solvolysis rates were slower than for VIII or IX. These decreases in rate are accounted for by steric inhibition of resonance by the two methyl groups, preventing the methoxy group from becoming planar with the aromatic ring. Hence racemization by nucleophilic displacement on the primary benzylic carbon by the ethyl methyl sulfide, was shown to be of minor importance.

Darwish and Tomlison (5), have investigated the racemization and solvolysis of phenacylethylmethylsulfonium

perchlorate, XIV.



XIV

Kenyon et al (3) showed that racemization of phenacylethylmethylsulfonium iodide involved a displacement of ethyl methyl sulfide by a reversible nucleophilic attack on carbon by the anion, as shown in Figure III.

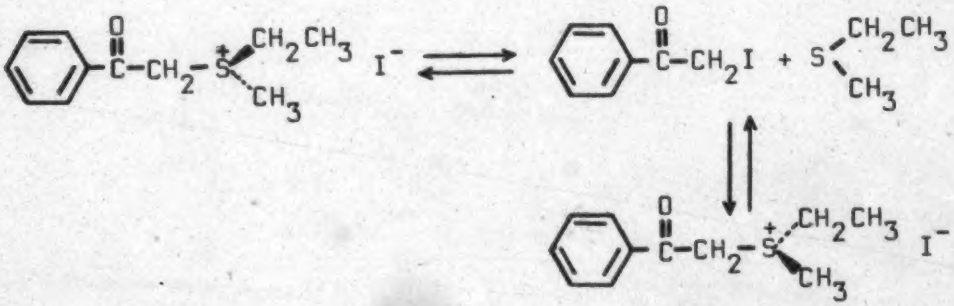
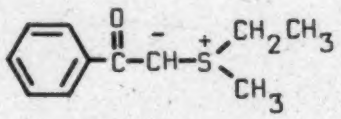


Figure III. Racemization via attack by a nucleophilic anion.

This mechanistic pathway is not possible with the perchlorate salt, because the perchlorate anion is non nucleophilic. Compound XIV was found to racemize 600X faster that it solvolyzed at 70° in anhydrous methanol, the loss of optical activity being due to racemization and not decomposition of the substrate. Racemization via carbon-sulfur bond heterolysis to yield an ion-neutral molecule pair can be dismissed, since it is energetically unfavourable.

The only mechanism which was consistent with the rate difference between solvolysis and racemization, and the observed products of solvolysis, was pyramidal inversion about the central sulfur atom.

Darwish and Tomlison (7), also investigated the racemization and decomposition of ethylmethylphenacylide, XV.



XV

Compound XV was found to racemize about 100X faster than it solvolyzed, the loss of optical activity again being due to racemization, and not decomposition of the substrate. The only reasonable mechanism to account for the racemization is by pyramidal inversion about the central sulfur atom.

This work also showed that compound XV racemized 200X faster than compound XIV in anhydrous methanol at 50^{0}. Two suggestions were put forward for this. Firstly the lone pair of electrons on the sulfur atom will have more s-character in the sulfonium salt than in the corresponding ylide, since the phenacylide group is more electropositive than the phenacyl group (8). As a result, the sulfur-alkyl bonds will have more p-character in the salt than in the ylide. A consequence of this will be that the ylide will have a more nearly planar configuration. Since the transition state

for pyramidal inversion is planar, one would expect that the energy of activation would be correspondingly less for the ylide than for the salt, enabling it to racemize at a faster rate. The second suggestion is that p-dπ bonding might be better at the transition state for the ylide than at the ground state. Since the sulfonium salt is incapable of this type of stabilization of the transition state, this may also explain the faster rate of racemization for the ylide.

This thesis presents the preparation of several optically active sulfonium perchlorate salts in which aryl groups were attached directly to the central sulfur atom. Racemization via carbon-sulfur bond heterolysis to form an ion - neutral molecule pair is a highly unlikely process in the systems studied, as is nucleophilic displacement by the anion, due to the extremely weak nucleophilicity of the perchlorate ion. Consequently we would expect the mechanism of racemization to be one involving pyramidal inversion.

In the systems studied there is the possibility of resonance interaction between the aromatic ring and the positive charge on sulfur, consequently, electronic effects may play a part in the racemization process.

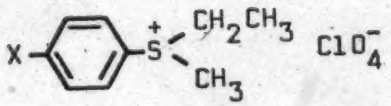
Steric effects on the rates of solvolysis and racemization have also been investigated by the introduction of bulkier groups around the central sulfur atom. Attempts to prepare optically active acyclic triaryl sulfonium salts

were unsuccessful. However, results from the monoaryl and diaryl systems can give us an estimate of the half-lives for racemization of these compounds.

CHAPTER I

MONOARYL SULFONIUM SALTS

This chapter describes the synthesis and resolution of several monoaryl sulfonium salts. Electronic effects upon the racemization process were investigated by introducing various groups into the para position of the benzene ring. The effect of both electron donating and electron withdrawing groups will be discussed. The solvolysis and racemization rates of the following systems were studied:



I, X=H

II, X=OCH_3

III, X=OH

IIIA, X=O^-

IV, X=NO_2

Data has also been obtained on the isopropylethylmethyl system, V. Since an isopropyl group is similar in size to a phenyl group, then on steric grounds, the isopropylethylmethyl and phenylethylmethylsulfonium systems should exhibit similar racemization rates, if pyramidal inversion is the mechanism.

Tentative data has also been obtained on the cyclohexylethylmethyl system, VI. The optically active

perchlorate salts were isolated as oils, all attempts to obtain crystalline materials were unsuccessful. No elemental analysis was done, and although clear, colorless oils were obtained, their purity is suspect.

SYNTHESIS AND RESOLUTION

All the salts, with the exception of the isopropylethylmethyl system, were prepared by the same general procedure. This involved preparation of the appropriate sulfide, followed by reaction with Meerwein's Reagent (17), to yield racemic arylethylmethylsulfonium fluoroborate salts. Figure IV outlines the route used.

The isopropylethylmethyl system was prepared by reaction of isopropyl ethyl sulfide with methyl iodide, using acetone as solvent. Preparation of all sulfides, together with reaction conditions, are given in the experimental section.

Exchange of the fluoroborate anion was accomplished by conversion to the hydroxide, using a DOWEX 1-X8 anion exchange resin in its hydroxide ion form, followed by neutralization of the resulting sulfonium hydroxide with the appropriate acid. The optically active salts were obtained by resolution of the (-)-2R,3R-dibenzoylhydrogen tartrate salts. This proved to be unsuccessful for the cyclohexylethylmethyl system, resolution being finally achieved with α-bromo-π-camphorsulfonic acid. After separation of the

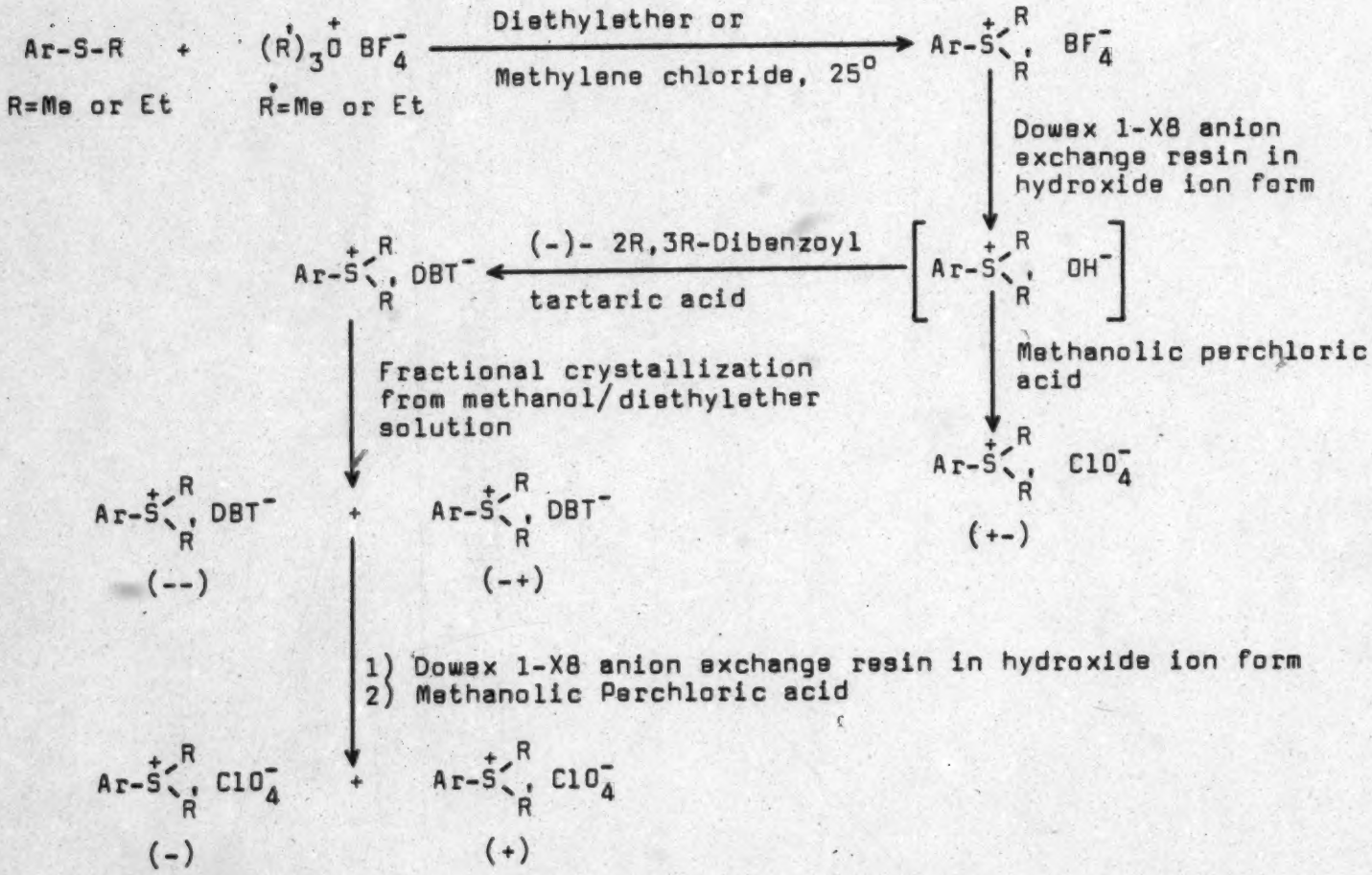


Figure IV. Synthesis and resolution of monoarylethylmethylsulfonium salts.

diastereoisomers, the optically active perchlorates were prepared by passage of the resolved 2R,3R-dibenzoylhydrogen tartrate salts through the anion exchange column, followed by neutralization of the eluent with 5% methanolic perchloric acid. The p-nitrophenylethylmethyl system was an exception. The 2R,3R-dibenzoylhydrogen tartrate salt was found to be almost insoluble in methanol, secondly, passage through the anion exchange resin resulted in some decomposition of the salt. Consequently, the perchlorate salts were prepared by direct titration of the 2R,3R-dibenzoylhydrogen tartrate salts with methanolic perchloric acid.

All compounds, except for the isopropylethylmethyl and cyclohexylethylmethyl systems gave satisfactory analyses. These, together with n.m.r. and i.r. spectra and melting points, are reported with the detailed synthetic procedures in the experimental section.

K. K. Anderson (9) has recently reported the synthesis of optically active p-tolylethylmethyl and p-tolylbutylmethylsulfonium salts, by treatment of alkoxysulfonium salts with dialkyl cadmium compounds.

SOLVOLYSIS STUDIES

The kinetics of the methanolysis of the monoaryl sulfonium perchlorate salts were studied by following the rate of appearance of acid. Each mole of sulfonium salt produces upon methanolysis one mole of acid.

The p-hydroxyphenylethylmethyl system was an exception. Two factors complicate the method employed for the other salts. Firstly, the methanolysis reaction was found to be very slow, secondly, the phenolic proton is also titrateable with base (sodium methoxide). For this latter reason, the methanolysis reaction was followed using ultra-violet spectroscopy.

Both the isopropylethylmethyl and cyclohexylethylmethylsulfonium perchlorates underwent very slow methanolysis at 90°. A rough estimate of the first order rate constants for both systems are given in Table I. All reactions followed first order kinetics. The titrimetric rate constants, k_t, were calculated from the relationship:

$$k_t = 2.303 \log \frac{V_\infty - V_o}{V_\infty - V_t}$$

where V_t is the titer at time t. Reactions were usually followed to ca. 85% completion, and a good straight line was obtained when the logarithm of $(V_\infty - V_t)$ was plotted against time t.

The first order methanolysis rate constants when the aryl group is phenyl, p-anisyl, and p-nitrophenyl, plus the approximate value for the cyclohexylethylmethyl and isopropylethylmethylsulfonium systems, are shown in Table I. A typical titrimetric rate analysis is shown in Table II. Figure V illustrates the corresponding kinetic plot of log $(V_\infty - V_t)$ vs. time.

TABLE I

SOLVOLYSIS OF RACEMIC ARYLETHYLMETHYLSULFONIUM PERCHLORATES, CYCLOHEXYLETHYLMETHYL AND ISOPROPYLETHYLMETHYLSULFONIUM PERCHLORATES IN ANHYDROUS METHANOL.

SYSTEM (R-X)[a]	TEMP	[SALT]	[2,6-LUTIDINE]	$10^6 k_t$ (sec^{-1})
Phenyl	90	0.0231	—	6.58 ± 0.07
Phenyl	90	0.0218	0.0497	6.51 ± 0.016
p-Anisyl	90	0.0199	—	1.54[b]
p-Anisyl	90	0.0187	0.0530	1.63[b]
p-Nitrophenyl	50	0.0205	0.0532	2.35 ± 0.007
p-Nitrophenyl	70	0.0212	0.0583	24.30 ± 0.90
Cyclohexyl	90	0.0376	—	ca. 0.1[c]
Isopropyl	90	0.0185	—	ca. 0.2[c]

a) X = $-\overset{+}{S}\begin{matrix}\diagup CH_3 \\ \diagdown CH_2CH_3\end{matrix}$

b) initial rates

c) only approximate values were obtained

TABLE II

METHANOLYSIS OF RACEMIC PHENYLETHYLMETHYLSULFONIUM PERCHLORATE IN THE PRESENCE OF 2,6-LUTIDINE AT 90.00°

[Salt]: 0.0218; [2,6-Lutidine]: 0.0497

Aliquot: 5.00 ml.; Titrant: $NaOCH_3$, 0.0365M

Indicator: Phenolphthalein

Theoretical infinity titer: 2.986 ml.

Experimental infinity titer: 2.855 ml.

TIME ($X10^4$ sec)	TITER (ml.)	log ($V_\infty - V_t$)	$10^6 k_t$ (sec^{-1})
0.00	0.03	0.4556	—
0.66	0.150	0.4527	6.59
1.35	0.250	0.4373	5.98
2.16	0.410	0.4101	6.67
2.97	0.509	0.3939	6.26
4.77	0.793	0.3410	6.60
6.57	1.037	0.2898	6.71
9.36	1.316	0.2227	6.49
12.06	1.571	0.1507	6.54
16.05	1.865	0.0494	6.53
20.16	2.134	$\bar{1}$.9304	6.78
		AVERAGE:	6.51 ± 0.016

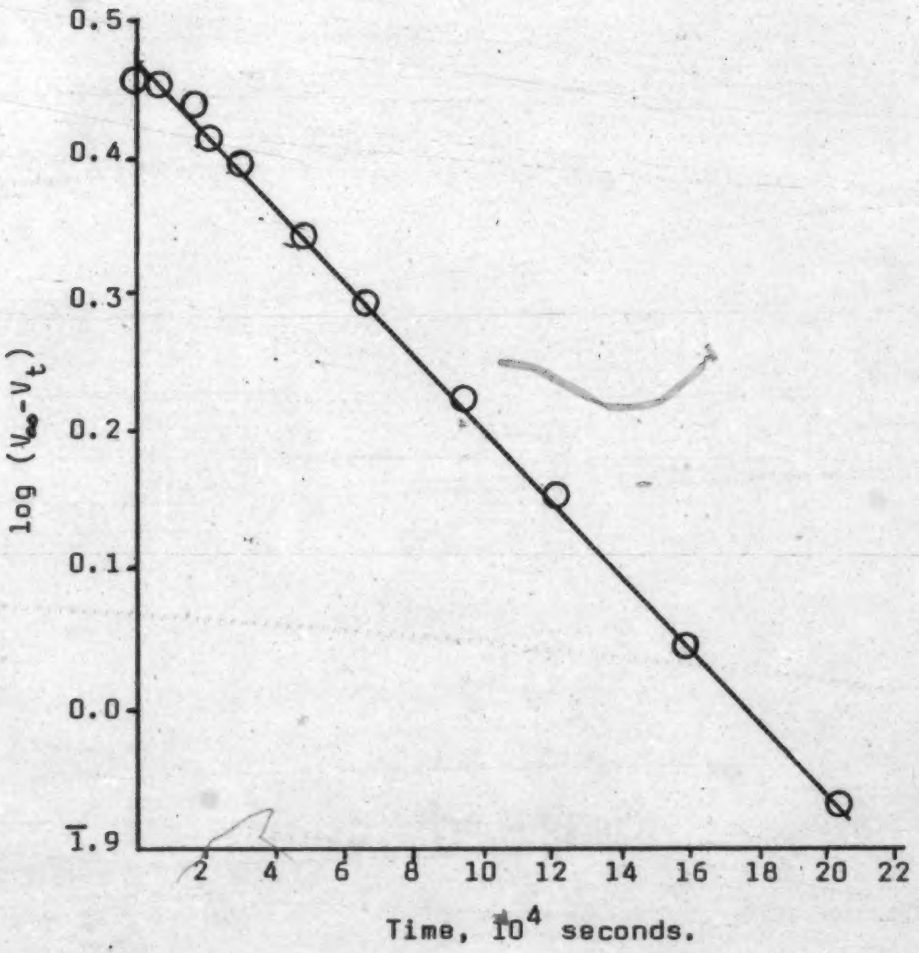


Figure V. Methanolysis of phenylethylmethylsulfonium perchlorate in the presence of 2,6-Lutidine at 90.00°.

SOLVOLYSIS OF p-HYDROXYPHENYLETHYLMETHYLSULFONIUM PERCHLORATE

As mentioned previously, two difficulties arose in the methanolysis of this salt. Firstly, the methanolysis was found to be extremely slow. This is to be expected, because of the resonance effect of the p-hydroxy group stabilizing the positive sulfur, making nucleophilic attack by solvent methanol less favorable than in the unsubstituted compound. The major difficulty however is that the methanolysis reaction cannot be followed by normal titration techniques, since the phenolic proton is also titrateable with base. An estimate of the rate was obtained using ultra-violet spectroscopy. The absorbances of the phenoxide ion form of the sulfonium salt, and phenoxide ion form of the sulfide produced in the methanolysis reaction are different. Consequently, if the reaction is quenched at appropriate time intervals, and the phenolic groups of the unreacted sulfonium salt and formed sulfide converted to the phenoxide ion forms with base, then the decrease in absorbance of the salt with time gives a rough measure of the rate. Precise details of the method are given in the experimental section. The results obtained are shown in Tables III and IV.

RACEMIZATION STUDIES

Racemization rates were obtained by following the disappearance of optical rotation with time. A Perkin-Elmer Model 141 Polarimeter, using incident light beams of

TABLE III

METHANOLYSIS OF *P*-HYDROXYPHENYLETHYLMETHYLSULFONIUM PERCHLORATE AT 90.00°

Perkin-Elmer Ultra-Violet - Visible Spectrophotometer Model 202

[Salt]: 0.0209

TIME ($\times 10^5$ sec)	$A_{279m\mu}$	CONCENTRATION ($\times 10^{-5}$ M)	$\log \frac{C_o}{C_t}$	$10^7 k_t$ [a] (sec^{-1})	%REACTION
0.0	1.365	7.58	—	—	0.0
1.725	1.225	6.81	0.0465	6.21	10.2
2.715	1.140	6.33	0.0783	6.64	16.5
3.654	1.090	6.06	0.0972	6.13	20.0
5.145	0.980	5.44	0.1441	6.45	28.2
6.867	0.870	4.83	0.1957	6.56	36.3
8.841	0.840	4.67	0.2103	5.48	38.4
11.238	0.770	4.28	0.2482	5.09	43.5
15.477	0.680	3.78	0.3022	4.50	50.1
27.465	0.560	3.11	0.3869	3.24	59.0

a) The rate constants decrease after *ca.* 36% reaction

TABLE IV

METHANOLYSIS OF P-HYDROXYPHENYLETHYLMETHYLSULFONIUM PERCHLORATE IN THE PRESENCE OF 2,6-LUTIDINE[a] AT 90.00°

Perkin-Elmer Ultra-Violet - Visible Spectrophotometer Model 202
[Salt] : 0.02094; [2,6-Lutidine] : 0.0651

TIME ($\times 10^5$ sec)	$A_{279m\mu}$	CONCENTRATION ($\times 10^{-5}$ M)	$\log \frac{C_o}{C_t}$	$10^7 k_t$ (sec^{-1})	% REACTION
0.0	1.33	7.39	—	—	0.0
1.728	1.17	6.50	0.0557	7.43	12.0
3.222	1.12	6.22	0.0749	5.35	15.8
4.242	1.05	5.86	0.1008	5.47	20.7
5.877	0.99	5.50	0.1283	5.03	25.6
7.728	0.84	4.67	0.1993	5.94	36.8
10.122	0.74	4.11	0.2548	5.80	44.4
11.889	0.69	3.83	0.2854	5.53	48.2
15.529	0.64	3.56	0.3172	4.70	51.8

a) 2,6-Lutidine absorbs strongly in the region 263 - 277mμ. The absorbance at 279mμ occurs on a steep portion of the curve, consequently, too much emphasis cannot be placed on the calculated figures.

436 mμ and 365 mμ, was employed. At these wavelengths, the optical rotation is larger than at the sodium D line (589 mμ), thus permitting a greater precision in the determination. Rates were run either using sealed ampoules (Method I), or the entire reaction was conducted in a thermostated polarimetric tube (Method II). The first order rate constants were calculated from the relationship:

$$k_{\alpha} = 2.303 \log \frac{\alpha_{\infty} - \alpha_0}{\alpha_{\infty} - \alpha_t}$$

where α_t is the rotation at time t. Reactions were usually followed to ca. 85% completion, and a good straight line was obtained when log $(\alpha_{\infty} - \alpha_t)$ was plotted against time t. Typical racemization rate analyses are shown is Tables V and VI. Figures VI and VII illustrate the corresponding kinetic plots of log $(\alpha_{\infty} - \alpha_t)$ vs. time.

The rate constant, k_1, the specific first order rate constant for the conversion of one enantiomer to another, can be calculated from the observed rate constants as follows:

$$k_1 = \tfrac{1}{2} (k_{\alpha} - k_t)$$

where k_{α} is the polarimetric rate constant, and k_t the titrimetric rate constant. Only in the p-nitrophenylethylmethyl system is k_t of any significance. Generally it can be assumed that:

$$k_1 = \tfrac{1}{2} k_{\alpha}$$

The results obtained are shown in Tables VII, VIII and IX.

TABLE V

RACEMIZATION OF (+)-PHENYLETHYLMETHYLSULFONIUM PERCHLORATE IN ANHYDROUS METHANOL AT 50.00°

Method II [Salt]: 0.0395

TIME ($X10^3$ sec)	$\alpha^{50}_{436m\mu}$	$\log (\alpha_\infty - \alpha_t)$	$10^5 k\alpha$ (sec^{-1})
0.0	+0.140	$\bar{1}.1461$	—
1.8	+0.133	$\bar{1}.1239$	2.85
3.6	+0.125	$\bar{1}.0969$	3.15
5.4	+0.119	$\bar{1}.0755$	3.01
7.2	+0.113	$\bar{1}.0531$	2.98
10.8	+0.102	$\bar{1}.0086$	2.93
12.6	+0.097	$\bar{2}.9868$	2.91
16.2	+0.087	$\bar{2}.9395$	2.94
19.8	+0.079	$\bar{2}.8976$	2.89
23.4	+0.072	$\bar{2}.8573$	2.84
27.0	+0.063	$\bar{2}.7993$	2.96
30.6	+0.058	$\bar{2}.7634$	2.88
66.9	+0.019	$\bar{2}.2788$	2.91
154.8	0.000	—	—
		AVERAGE:	2.94 ± 0.06

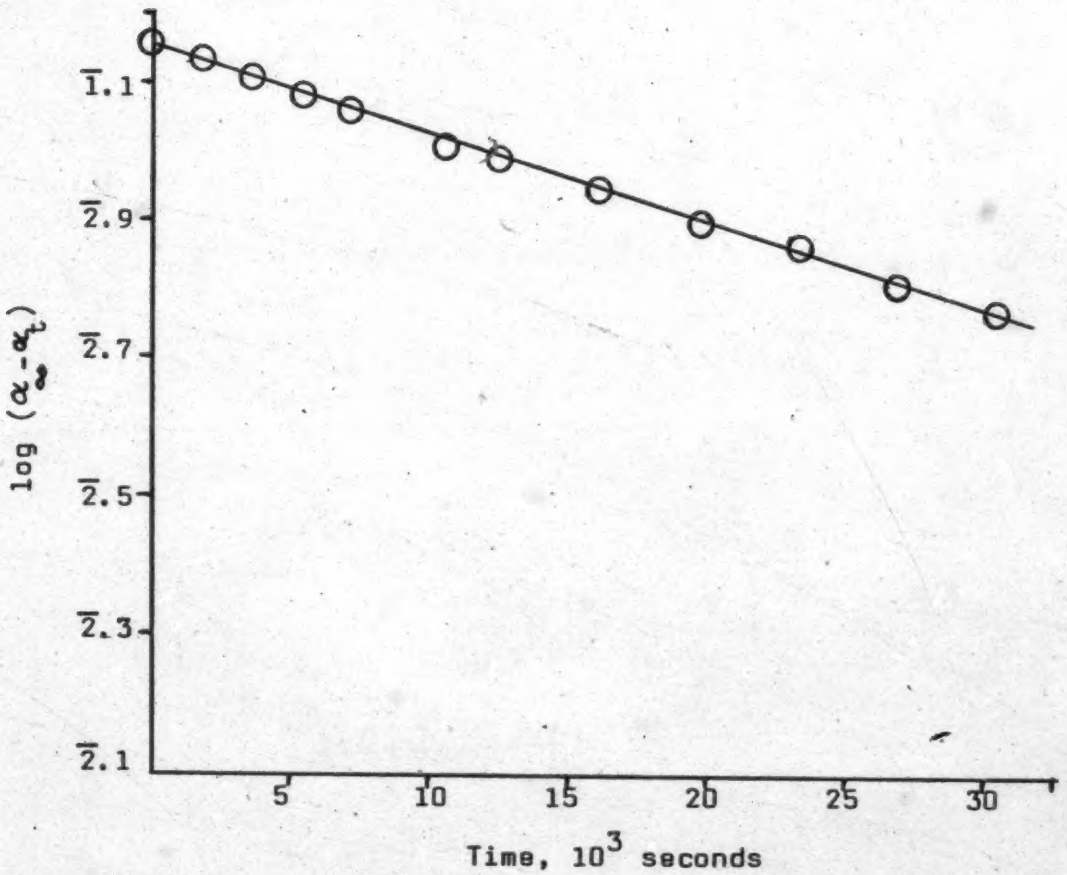


Figure VI. Racemization of (+)-Phenylethylmethylsulfonium perchlorate in anhydrous methanol at 50.00° (Method II).

TABLE VI

RACEMIZATION OF (-)-PHENYLETHYLMETHYLSULFONIUM PERCHLORATE IN ANHYDROUS METHANOL AT 50.00°

Method I [Salt]: 0.0303

TIME ($X10^3$ sec)	$\alpha^{50}_{436m\mu}$	$\log (\alpha_\infty - \alpha_t)$	$10^5 k_\alpha$ (sec^{-1})
0.0	-0.170	$\bar{1}.2304$	—
3.66	-0.152	$\bar{1}.1818$	3.06
7.62	-0.134	$\bar{1}.1271$	3.12
10.80	-0.126	$\bar{1}.1004$	2.77
14.40	-0.111	$\bar{1}.0453$	2.96
19.96	-0.097	$\bar{2}.9868$	2.83
26.10	-0.083	$\bar{2}.9191$	2.75
35.10	-0.064	$\bar{2}.8062$	2.78
42.30	-0.050	$\bar{2}.6990$	2.89
81.24	-0.017	$\bar{2}.2304$	2.83
259.20	0.000	—	—
		AVERAGE:	2.89 ± 0.11

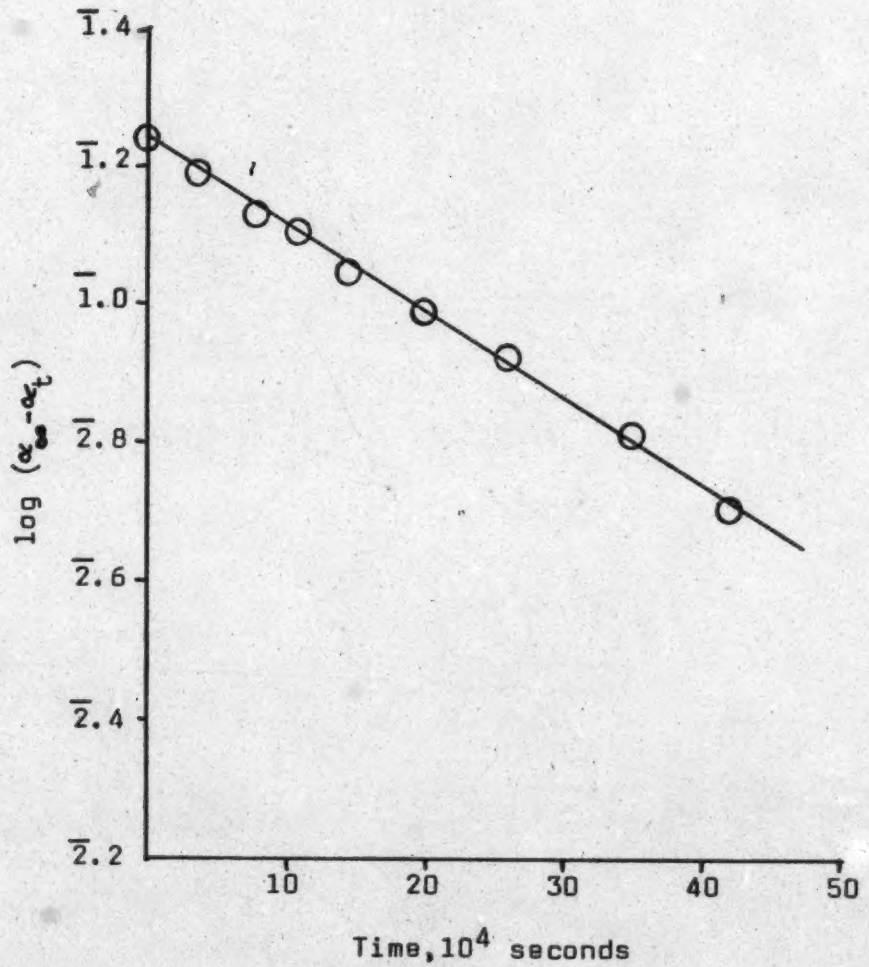


Figure VII. Racemization of (-)-Phenylethylmethylsulfonium perchlorate in anhydrous methanol at 50.00° (Method I).

TABLE VII

RACEMIZATION OF MONOARYLETHYLMETHYLSULFONIUM PERCHLORATES IN ANHYDROUS METHANOL

SYSTEM (Ar-X)[a]	TEMP	ISOMER	[SALT]	$10^5 k\alpha$ (sec^{-1})
Phenyl	50	+	0.0395	2.94 ± 0.06
Phenyl	50	-	0.0303	2.89 ± 0.11
Phenyl	70	-	0.0284	41.2 ± 1.6
Phenyl	90	-	0.0285	229 ± 25
Phenyl	90	+	0.0402	249 ± 24
Phenyl	25	+	0.0421	0.0739 ± 0.021
p-Anisyl	50	+	0.0348	4.80 ± 0.19
p-Anisyl	50	-	0.0297	4.62 ± 0.21
p-Anisyl	70	+	0.0293	57.8 ± 1.7
p-Nitrophenyl	50	-	0.0350	3.38 ± 0.14
p-Nitrophenyl	50	+	0.0306	3.43 ± 0.05
p-Nitrophenyl	70	+	0.0335	45.0 ± 0.6

a) X = $S^+(CH_3)(CH_2CH_3)$

TABLE VIII

RACEMIZATION OF ISOPROPYLETHYLMETHYL[a,b] AND CYCLOHEXYLETHYLMETHYLSULFONIUM[a] PERCHLORATES IN ANHYDROUS METHANOL

SYSTEM (R-X)[c]	TEMP	ISOMER	[SALT]	$10^5 k_\alpha$ (sec^{-1})
Isopropyl	50	-	0.0613	4.44 ± 0.12
Cyclohexyl	50	+	0.0456	8.55 ± 0.18
Cyclohexyl	50	-	0.0531	8.50 ± 0.84
Cyclohexyl	25	+	0.0492	0.245 ± 0.002

a) Neither salt could be obtained as a crystalline solid. and both gave poor elemental analyses.

b) only one isomer could be obtained

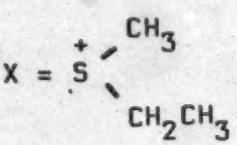
c) X = 

TABLE IX

RACEMIZATION OF P-HYDROXYPHENYLETHYLMETHYLSULFONIUM PERCHLORATE IN ANHYDROUS METHANOL UNDER VARIOUS CONDITIONS

TEMP	ISOMER	[SALT]	[2,6-LUTIDINE]	[$NaOCH_3$]	[$HClO_4$]	$10^5 k_\alpha$ (sec^{-1})
50	+	0.0345	—	—	—	5.16 ± 0.08
50	+	0.0464	0.0585	—	—	5.26 ± 0.16
50	+	0.0340	—	0.0365	—	12.02 ± 0.15
50	+	0.0345	—	0.122	—	12.28 ± 0.38
50	+	0.0354	—	—	0.0405	5.30 ± 0.11
50	+	0.0355	—	—	0.122	4.99 ± 0.17
70	-	0.0397	—	—	0.140	68.3 ± 1.6
70	-	0.0293	—	0.0355	—	145 ± 9.5

DISCUSSION

The methanolysis rate constants vary with the nature of the group in the para position of the benzene ring. Electron withdrawing groups increase the rate, whereas electron donating groups decrease the rate, compared to the unsubstituted compound. This is consistent with a mechanism involving carbon-sulfur bond heterolysis, to yield the aryl alkyl sulfide and an ether, as shown in Figure VIII.

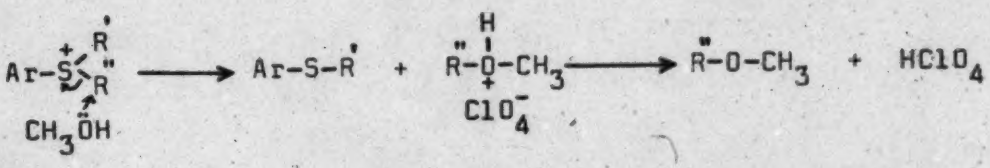


Figure VIII. Possible methanolysis mechanism for arylethylmethylsulfonium perchlorates.

The reaction takes place presumably via a concerted mechanism, since formation of ethyl or methyl carbonium ions is energetically unfavorable. Electron withdrawing groups in the para position of the benzene ring will increase the positive nature of the sulfur, facilitating attack by the solvent. Electron donating groups will decrease the positive nature of the sulfur, inhibiting attack by the solvent.

A comparison of the solvolysis and racemization rate constants for each compound shows that only in the p-nitrophenylethylmethyl system IV, is solvolysis playing a part in the racemization process. However, even then,

only about 10.5% solvolysis has occurred when the salt is completely racemized. Thus the assumption can be made, that for the systems studied, excluding IV;

LOSS OF OPTICAL ACTIVITY = $k_{\alpha} = 2k_1$.

Similarly, for the isopropylethylmethyl, V, and cyclohexylethylmethyl, VI, systems, racemization was found to be very much faster than solvolysis.

For all compounds reported, excluding compound IV, we find:

$$\frac{k_{\alpha}}{k_t} > 300$$

so $k_{rac} = k_{\alpha}$ within 0.3%.

The relative rates of racemization in solvent methanol at 50° are as follows:

I	II	III	IIIA	IV	V	VI
1	1.61	1.86	4.17	1.19	1.54	2.97

One feature is clear from the relative rate data, that is, aryl groups do not have an appreciable electronic effect upon the rate of racemization. A comparison of II, III and IV with I, shows that introduction of a p-methoxy, p-hydroxy or p-nitro group into the benzene ring, leads to an increase in the rate of racemization of less than a factor of 2. Unlike the solvolysis data, both electron withdrawing and electron donating groups increase the rate of racemization by small amounts, thus eliminating a racemization mechanism via carbon-sulfur bond heterolysis.

In the presence of one equivalent of sodium methoxide in methanol, compound III is converted to the corresponding zwitterion (p-O^-), this dipolar species was in fact isolated as a solid in optically active form, IIIA. This compound racemized only 4.2X faster than I, again confirming that any electronic effect associated with substitution on the aromatic ring is small.

Darwish and Tourigny (4), in their study of the t-butylethylmethylsulfonium system showed that any increases in racemization rate, obtained by placing substituents in the 1-position of the t-butyl group, could be explained in terms of steric effects, and not electronic effects. Good evidence was obtained for a racemization process involving pyramidal inversion about the central sulfur atom. Similarly, a study of the benzylethylmethylsulfonium system (5,6), in which substituents were introduced into the meta and para positions of the benzene ring, showed that the major portion of the racemization process could be accounted for by pyramidal inversion. Again, electron donating and electron withdrawing groups were found not to affect the rate of racemization significantly. Darwish and Tomlison (5), also found phenacylethylmethylsulfonium perchlorate to racemize 600X faster than it solvolyzed, in methanol at 70°. In the same communication (5), it was pointed out that the benzylethylmethyl system racemized only twice as fast as the phenacylethylmethyl system. This is not surprising, since non-bonded interactions would be expected to be very similar in both systems. The

result also indicates that any electronic effects are very small, if present at all.

The t-butylethylmethyl system racemizes much faster than the phenacylethylmethyl system, this is consistent with the t-butyl group being much larger than the phenacyl group, causing a steric acceleration of rate. The non-bonded interactions in the phenylethylmethyl system will be greater than in either the phenacylethylmethyl or benzylethylmethyl systems, consequently, an increase in rate would be expected on steric grounds. However, the t-butyl group is larger than a phenyl group, consequently, the phenylethylmethyl system would be expected to racemize slower, which is observed. The results are shown for comparison in Table X.

The isopropyl and cyclohexyl groups are similar in size to a phenyl group, and a consideration of the non-bonded interactions would lead to a prediction of similar rates of racemization for the isopropylethylmethyl, V, and cyclohexylethylmethyl, VI, systems, if pyramidal inversion is the mechanism. The relative rates of racemization in anhydrous methanol at 50° for I : V : VI, are 1 : 1.54 : 2.97. The results indicate that some steric effect is in operation in the cyclohexylethylmethyl system.

Darwish and Tomlison (7), removed a methylinic proton from the phenacylethylmethylsulfonium system which resulted in formation of a sulfonium ylide, Figure IX. This was later isolated in optically active form.

TABLE X

A COMPARISON OF THE RACEMIZATION RATES OF VARIOUS SYSTEMS AT 50.00°.

SYSTEM (R-X)[a]	SOLVENT	$10^6 k_{\alpha}^{50}$ (sec^{-1})
Phenacyl[b]	anhyd. methanol ($3X10^{-3}$M $HClO_4$)	3.7
Benzyl[b]	anhyd. methanol	6.0
Phenyl	anhyd. methanol	30.0
t-Butyl[c]	anhyd. methanol	440.0

a) X = S^{+}(CH$_3$)(CH$_2$CH$_3$)

b) Reference 5

c) Reference 4

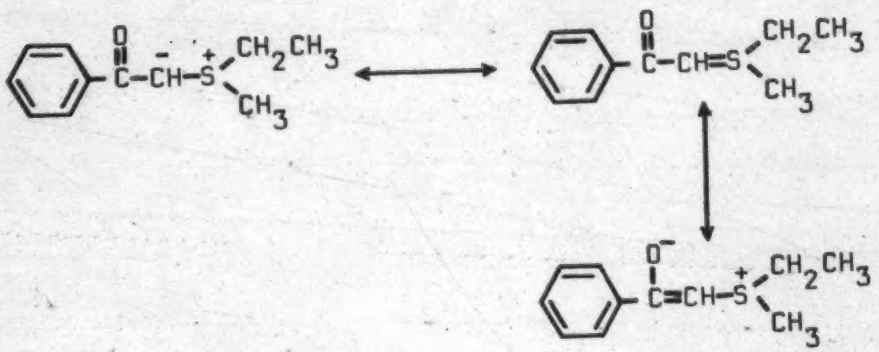


Figure IX. Resonance forms of ethylmethylphenacylide.

The ylide was found to racemize 200X faster than the sulfonium salt in methanol at 50°. Two possible explanations were put forward for this, both of which have already been outlined in the introduction.

One explanation was that p-dπ bonding might be better in the transition state for the ylide than in the ground state. The sulfonium salt is incapable of this type of stabilization of the transition state, and hence a higher barrier to inversion might be expected. In the arylethylmethyl system, there is the possibility of direct resonance interaction between the ring and the positively charged sulfur atom via p-dπ overlap. If stabilization of the transition state via p-dπ bonding occurred in these systems, then it might be expected that electron donating groups would increase the racemization rate, relative to the unsubstituted compound, whereas electron withdrawing groups would decrease the rate, relative to the unsubstituted compound. From the results,

it can be concluded that stabilization of the transition state by resonance is very small, if present at all. A further possibility is that stabilization by resonance is just as likely to occur in the ground state as it is in the transition state. In any molecule where sulfur is surrounded by groups in a tetrahedral arrangement, π-bonding can occur between suitable orbitals of the surrounding groups and the sulfur orbitals, $d_{x^2-y^2}$ and d_{z^2} (10). These orbitals are more favorable for π-bonding than the other d-orbitals of sulfur, both geometrically and energetically. Consequently, the p_z-orbital of the carbon atom on the ring, adjacent to the sulfur, can participate in p-dπ overlap with either orbital of the sulfur in the ground state. In the planar transition state for pyramidal inversion, the two d-orbitals of sulfur which are geometrically more favorable for p-dπ overlap are the d_{xz} and d_{xy} orbitals. Although the d_{xy} orbital is higher in energy than the d_{xz} orbital, p-dπ overlap might be expected to be at least as favorable in the transition state as in the ground state.

The largest increase in racemization rate was observed with the p-phenoxyethylmethyl system. The phenolic proton in the p-hydroxyphenylethylmethylsulfonium system is readily removed by addition of a strong base such as sodium methoxide. Using ultra-violet spectroscopy, the p-hydroxyphenylethylmethylsulfonium perchlorate was found to exist in both phenol and phenoxide ion forms in solvent methanol.

The spectroscopic data for the salt under various conditions is shown in Table XI. The absorbances and extinction coefficients without any added acid or base are estimates obtained from the spectra. Using these values, and the absorbances of the compound in the presence of large excesses of acid and base (i.e., completely in phenolic and phenoxide ion forms), the concentration of the dissociated and undissociated species in methanol were calculated. The salt was found to be ca. 45% dissociated, with a pKa value of 4.55.

Bordwell and Boutan (11), have investigated the acidity of p-hydroxyphenyldimethylsulfonium p-toluenesulfonate and p-bromobenzenesulfonate salts, obtaining a pKa value of 7.30 in water at 25^{o}, in both cases. They also found the p-hydroxyphenyldimethylsulfonium salt to be about twice as acidic as the m-hydroxyphenyldimethylsulfonium salt, suggesting that the greater acidity is best accounted for by assuming a conjugative interlocking between the $-\overset{+}{S}-(CH_3)_2$ and $-O^-$ groups.

The p-hydroxyphenylethylmethyl system is of special interest, since removal of the phenolic proton should result in formation of a dipolar species, as shown in Figure X.

(see over, Figure X.)

Passage of a methanolic solution of optically active p-hydroxyphenylethylmethylsulfonium perchlorate through a Dowex 1-X8 anion exchange resin in hydroxide ion form, removing the solvent methanol, and pumping the oily residue under

TABLE XI

U.V. DATA FOR P-HYDROXYPHENYLETHYLMETHYLSULFONIUM PERCHLORATE UNDER VARIOUS CONDITIONS IN ANHYDROUS METHANOL AS SOLVENT.

[SALT] ($X10^{-5}$)	[$HClO_4$] ($X10^{-5}$)	[$NaOCH_3$] ($X10^{-5}$)	A(-OH) (247-249mμ)	A($-O^-$) (279-280mμ)	ε(-OH)	ε($-O^-$)
7.5	—	—	0.62	0.61	15,000 (4.18)[a]	18,000 (4.26)[b]
7.1	—	7.3	—	1.17	—	16,480 (4.22)[b]
8.1	—	24.4	—	1.44	—	17,777 (4.25)[b]
7.5	—	2440.0	—	1.36	—	18,133 (4.26)[b]
7.6	16.2	—	1.085	—	14,370 (4.16)[a]	—
7.1	24.4	—	1.07	—	15,070 (4.18)[a]	—
7.5	4050.0	—	1.13	—	15,060 (4.18)[a]	—

a) log ε(-OH)

b) log ε($-O^-$)

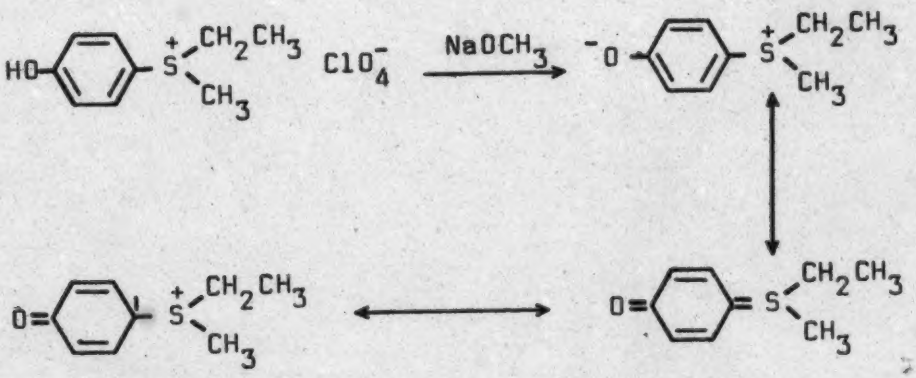


Figure X. Formation and resonance forms of the dipolar species from p-hydroxyphenylethylmethylsulfonium perchlorate.

vacuum, yielded an optically active white solid. The solid was found to be very soluble in hydroxylic solvents yielding a basic solution, however it was insoluble in chloroform, carbon tetrachloride, acetone and dimethylsulfoxide. Attempts to determine the exact structure of the material were unsuccessful, full details of the experiments performed are given in the Experimental. Racemization rates run on the material are shown in Table XII. The rates at 50.00° and 70.00° in anhydrous methanol as solvent are, within experimental error, identical with those obtained for the p-hydroxyphenylethylmethylsulfonium perchlorate salt, when run in the presence of sodium methoxide (Table IX). It is noteworthy that even under these conditions of a strong electron donating group, only a four fold increase in rate is observed over the unsubstituted compound, giving further evidence that electronic effects in the racemization of arylethylmethylsulfonium salts

TABLE XII

RACEMIZATION OF DIPOLAR SPECIES PREPARED FROM OPTICALLY ACTIVE P-HYDROXYPHENYLETHYLMETHYLSULFONIUM PERCHLORATE

SOLVENT : Anhydrous Methanol

ISOMER	TEMP	CONCENTRATION (g/10 ml)	$10^5 k_\alpha$ (sec^{-1})
+	25	0.0921	0.399 ± 0.011
+	50	0.1022	11.90 ± 0.15
+	70	0.1040	144.0 ± 6.0

are small.

The results of substituent effects on the relative rates of racemization of arylethylmethylsulfonium salts indicate that racemization occurs almost exclusively via inversion about the central sulfur atom. Carbon-sulfur bond heterolysis is a highly unlikely process, formation of a carbonium ion - neutral molecule pair being energetically unfavorable. Electronic effects are small, both electron donating and electron withdrawing groups increasing the rate slightly. Stabilization of the transition state relative to the ground state via p-dπ bonding between the ring and the positively charged sulfur cannot be discounted, especially in the p-phenoxyethylmethyl system, but the effect is small if present at all.

TEMPERATURE EFFECTS ON RACEMIZATION

Increasing the temperature increases the racemization rate. To determine the effect of temperature on the rate, the Arrhenius equation was employed:

$$k = e^{-Ea/RT}.$$

For reactions in solution, the heat of activation is given by (12):

$$\Delta H^{\ddagger} = Ea - RT \text{ kcal/mole.}$$

The entropy of activation, $\Delta S^{\ddagger}$, is derived from the equation (12):

$$k = k_B \frac{T}{h} \cdot e^{\Delta S^{\ddagger}/R} \cdot e^{-\Delta H^{\ddagger}/RT}.$$

where k_B is Boltzman's constant and h is Planck's constant. Thus at 50°:

$$\Delta S^{\ddagger} = 4.576 \left(\log k_1^{50^{\circ}} - 12.79 + \frac{\Delta H^{\ddagger}}{4.576 \times 10^{-3}\ T}\right) \text{ e.u.}$$

where k_1 is the specific first order rate constant for the conversion of one enantiomer to the other.

Results for the activation parameters are given in Table XIII.

TABLE XIII

ACTIVATION PARAMETERS FOR RACEMIZATION OF THE MONOARYL-ETHYLMETHYL SYSTEMS AT 50.00°.

Ar-X[a]	$\Delta H^{\ddagger}$ (kcal/mole)	$\Delta S^{\ddagger}$ (e.u.)
Phenyl	27.5 ± 0.4	4.1 ± 1.2
p-Anisyl	27.3 ± 0.8	4.5 ± 2.7
p-Hydroxyphenyl	28.8 ± 0.5	9.1 ± 1.8
p-Phenoxy	26.5 ± 0.4	3.8 ± 1.5
p-Nitrophenyl	28.2 ± 0.3	6.5 ± 1.2

a) X = S^{+} (with CH_3 and CH_2CH_3)

EXPERIMENTAL

PHYSICAL MEASUREMENTS

All melting points and boiling points are uncorrected. Melting points were taken on a Hershberg melting point apparatus, using a set of Anschutz thermometers.

Refractive indices were recorded on a Bausch and Lomb Abbe - 3L Refractometer which was thermostated at 25°.

Infrared spectra were recorded on a Perkin-Elmer Infrared Spectrophotometer, model 421, using sealed sodium chloride cells.

Nuclear magnetic resonance spectra were recorded on Varian analytical Spectrophotometers, models A-60 and A 56/60, and on a Varian HA-100.

Ultra-violet spectra were obtained using a Perkin-Elmer Ultra-violet - Visible Spectrophotometer, model 202.

Optical rotation measurements were obtained on a Perkin-Elmer Polarimeter, model 141.

Elemental analyses were performed by Mrs. D. Mahlow and Mrs. A. Dunn.

SOLVENTS, REAGENTS AND MATERIALS

Anhydrous methanol

This was prepared by Lund and Bjerrum's method from commercially available reagent methanol (maximum water 0.02%) by treatment with magnesium methoxide, as described by Fieser (13), b.p. 63° at 705 mm. A Karl Fischer titration (14) was performed, and showed that the solvent contained less than 0.001% water.

2,6-Lutidine

Eastman Practical Grade 2,6-Lutidine was dried over potassium hydroxide for several days, followed by refluxing over and distillation from barium oxide, as described by Fieser for the preparation of anhydrous pyridine (15). The centre cut from this distillation was treated with boron trifluoride as described by Brown et al (16). Pure 2,6-Lutidine was then fractionally distilled from this mixture, b.p. 139-141° at 705 mm. n_D^{25} 1.4954 (reported (16): b.p. 143° at 760 mm., n_D^{25} 1.4953).

Standard sodium methoxide solution for titrations

A weighed amount of freshly cleaned sodium was added to one gallon of Reagent Grade Methanol. The resulting solution was standardized with Fisher Certified Primary Standard potassium hydrogen phthalate in water, using phenolphthalein as indicator. Restandardization showed the

solution to be stable for at least two years when it is stored in a tightly-stoppered dark bottle.

Triethyloxonium fluoroborate

Prepared as described by H. Meerwein (17). No analysis was done.

Trimethyloxonium fluoroborate

Prepared as described by H. Meerwein (17). No analysis was done.

(-)-2R,3R-Dibenzoyl tartaric acid monohydrate

Prepared as described by Butler (18).

Phenyl methyl sulfide

Prepared by the method of Barnard, McFabian and Koch (19).

Yield: 89%. b.p. 60-62° at 6 mm. (reported (19): 80° at 16.5 mm.). n_D^{25} 1.5833 (reported (19): n_D^{25} 1.5870). N.m.r. (neat): τ 7.84 (s,3H), 2.80-3.18 (m,5H). Infrared (neat): 684, 730, 950, 960, 1020, 1082, 1436, 1578, 2920, 3020, 3060, 3070 cm^{-1}.

Phenylethylmethylsulfonium fluoroborate

A 20 g. (0.16 mole) quantity of phenyl methyl sulfide was dissolved in 50 ml. of diethylether in a 500 ml. round bottomed flask fitted with a drying tube. The flask

was flushed with nitrogen gas and 35 g. (0.18 mole) of triethyloxonium fluoroborate was added. The flask was again flushed with nitrogen, the drying tube replaced, and the mixture stirred magnetically. The reaction was allowed to proceed overnight, after which time an oil had been produced, insoluble in ether.

Crystallization of the oil from methanol/diethylether solution resulted in formation of a slightly hygroscopic white solid. The salt was recrystallized a further 2X from methanol/diethylether solutions.

Yield: 80%. m.p. 31.5-33.5° (dec.) N.m.r. (dimethylsulfoxide-$\underline{d}_6$): τ8.70 (t,3H,J=7.5 c.p.s.), 6.59 (s,3H), 6.00-6.46 (q,2H), 1.68-2.50 (m,5H). The quartet was split due to the methylene group's being adjacent to an assymetric centre This was found to be so for all the systems studied. Infrared (nujol): 685, 755, 760, 995, 1030-1090, 1424, 1445 cm^{-1}.

Phenylethylmethylsulfonium 2R,3R-dibenzoylhydrogen tartrate

A 30 g. (0.125 mole) quantity of phenylethylmethylsulfonium fluoroborate was dissolved in a minimum quantity of reagent methanol and passed through a Dowex 1-X8 anion exchange resin in hydroxide ion form. The column was eluted with methanol until the eluent no longer gave a basic test with phenolphthalein indicator. The eluent was allowed to drip into a solution of 47.0 g. (0.125mole) of (-)-2R,3R-

dibenzoyl tartaric acid, dissolved in diethylether. After the exchange was complete, the solvent was stripped off on the rotary evaporator until the volume had been considerably reduced. Diethylether was then added, producing precipitation of a white solid.

Yield: 95%. m.p. 107-109°. $[\alpha]_D^{25}$ - 105.9° (c 0.1020, anhyd. methanol). N.m.r. (dimethylsulfoxide-d_6): τ8.92 (t,3H,J=7.5 c.p.s.), 6.70 (s,3H), 6.08-6.57 (q,2H), 4.26 (s,2H), 1.75-2.92 (m,15H), -1.5 (s,1H). Infrared (nujol): 1260, 1710, 2840-2960 cm^{-1}.

Anal. Calcd. for $C_{27}H_{26}O_8S$: C, 63.50; H, 5.10; S, 6.27.
Found: C, 63.29, 63.45; H, 4.96, 5.10; S, 6.11, 6.56.

The salt was resolved by fractional crystallization from methanol/diethylether solution. After dissolving the salt in methanol, diethylether was added dropwise from a teat pipette until crystallization just occurred. The flask was cooled to 5° and left overnight. The mother liquor was then carefully poured off and the remaining crystals collected and washed well with diethylether. Addition of diethylether to the mother liquor resulted in precipitation of the other diastereoisomer. The same general procedure was used for subsequent systems. However, it should be pointed out that the point at which crystallization first occurs is a nebulous one, and several attempts were usually needed to obtain separation.

Racemic phenylethylmethylsulfonium perchlorate

A 10 g. (0.042 mole) quantity of phenylethylmethylsulfonium fluoroborate was dissolved in methanol, and passed through a Dowex 1-X8 anion exchange resin in hydroxide ion form, using methanol as the eluate. When elution was complete, as indicated by a negative test for basicity with phenolphthalein, the eluent was neutralized with a 10% methanolic solution of perchloric acid to a pH of approximately 8. The solvent was removed on a rotary evaporator until the volume had been considerably reduced. Diethylether was then added to the cloud point, and the flask cooled to -10°. The resulting white crystals were filtered and recrystallized 2X from methanol/diethylether solutions, then dried in vacuo.

Yield: 86%. m.p. 75.2-76.2°. N.m.r. (dimethylsulfoxide-d_6): τ8.92 (t,3H,J=7.5 c.p.s.), 6.80 (s,3H), 6.20-6.67 (q,2H), 1.92-2.58 (m,5H). Infrared (nujol): 682, 752, 760, 1055-1105, 1442, 1475, 2840-2980 cm^{-1}.

Anal. Calcd. for $C_9H_{13}O_4SCl$: C, 42.80; H, 5.15.

Found: C, 42.96, 42.52; H, 5.06, 5.36.

(+)-Phenylethylmethylsulfonium perchlorate

A 10 g. (0.02 mole) quantity of the first crop of crystals obtained from the resolution of the 2R,3R-dibenzoylhydrogen tartrate salt, was dissolved in methanol and passed through the anion exchange resin in the usual manner. The

eluent was neutralized with a 10% methanolic solution of perchloric acid to a pH of approximately 8. After work-up, a white solid was obtained which was recrystallized 2X from methanol/diethylether solutions.

Yield: 89%. m.p. 74.8-75.8°. $[\alpha]_{436}^{25}$ + 10.0° (c 1.209, anhyd. methanol). N.m.r. (dimethylsulfoxide-d_6): τ8.74 (t,3H,J=7.5 c.p.s.), 6.61 (s,3H), 6.01-6.51 (q,2H), 1.72-2.41 (m,5H). Infrared (nujol): 682, 752, 760, 1055-1105, 1442, 1475, 2840-2980 cm^{-1}.

Anal. Calcd. for $C_9H_{13}O_4SCl$: C, 42.80; H, 5.15.
Found: C, 42.94, 43.14; H, 5.40, 5.63.

(-)-Phenylethylmethylsulfonium perchlorate

A 10 g. (0.02 mole) quantity of the crystals obtained from the mother liquor in the resolution of the 2R,3R-dibenzoylhydrogen tartrate salt was converted to the optically active perchlorate salt as described for the (+) isomer.

Yield: 90%. m.p. 80.5-82.0°. $[\alpha]_{436}^{25}$ - 17.0° (c 1.100, anhyd. methanol). N.m.r. (dimethylsulfoxide-d_6): τ8.74 (t,3H,J=7.5 c.p.s.), 6.62 (s,3H), 6.03-6.51 (q,2H), 1.73-2.33 (m,5H). Infrared (nujol): 682, 752, 760, 1055-1105, 1442, 1475, 2840-2980 cm^{-1}.

Anal. Calcd. for $C_9H_{13}O_4SCl$: C, 42.80; H, 5.15.
Found: C, 43.06, 42.68; H, 5.44, 5.50.

para-Methoxythiophenol

Prepared by the method of Suter and Hansen (20). Yield: 63%. b.p. 67-69° at 0.5 mm. (reported (20): 88-89° at 5 mm.). n_D^{25} 1.5786 (reported (20): 1.5801). N.m.r. (neat): τ6.82 (s,1H), 6.78 (s,3H), 3.46-3.84 (m,2H), 3.00 -3.34 (m,2H). Infrared (neat): 818, 1030, 1242, 1282, 1490 cm^{-1}.

para-Anisyl methyl sulfide

Prepared by the method of Gilman and Beaber (21). Yield: 98%. b.p. 85-86° at 0.4 mm. (reported (21): 239-240° at 760 mm.). n_D^{25} 1.5754 (reported (21): 1.5764). N.m.r. (neat): τ7.68 (s,3H), 6.49 (s,3H), 3.06-3.38 (m,2H), 2.58 -2.92 (m,2H). Infrared (neat): 820, 1030, 1240, 1284, 1438, 1460, 1590 cm^{-1}.

para-Anisylethylmethylsulfonium fluoroborate

A 17 g. (0.11 mole) quantity of p-anisyl methyl sulfide was placed in a 500 ml. round bottomed flask fitted with a drying tube. After flushing out the flask with nitrogen, 25 g. (0.128 mole) of triethyloxonium fluoroborate, together with 25 ml. of diethylether were added. The flask was again flushed with nitrogen, the drying tube replaced, and the mixture magnetically stirred. The following day a white solid had been formed. This was filtered and re-crystallized from methanol/diethylether solution.

Yield: 85%. m.p. 65.5-66.5°. N.m.r. ($CDCl_3$): τ8.68 (t,3H,

J=7.5 c.p.s.), 6.73 (s,3H), 6.18-6.60 (q,2H), 6.11 (s,3H), 2.70-2.96 (m,2H), 1.98-2.20 (m,2H). Infrared (nujol): 1010-1085, 1260, 1455, 2850, 2920, 2950 cm^{-1}.

para-Anisylethylmethylsulfonium 2R,3R-dibenzoylhydrogen tartrate

A 12 g. (0.044 mole) quantity of p-anisylethylmethylsulfonium fluoroborate was dissolved in a minimum amount of methanol and converted to the 2R,3R-dibenzoylhydrogen tartrate salt, as described for the unsubstituted salt. After work-up a white solid was obtained which was recrystallized from methanol/diethylether solution. Yield: 99.5%. m.p. 125.8-126.8°. $[\alpha]_D^{25}$ - 82.4° (c 1.009, anhyd. methanol). N.m.r. (dimethylsulfoxide-d_6): τ8.89 (t,3H,J=7.5 c.p.s.), 6.71 (s,3H), ca. 6.13-6.62 (q,2H), 6.13 (s,3H), 4.25 (s,2H), 1.75-2.92 (m,14H). Infrared (nujol): 1268. 1448, 1458, 1712, 2840, 2930 cm^{-1}.

The salt was resolved by fractional crystallization from methanol/diethylether solution, as described for the unsubstituted compound.

Racemic para-Anisylethylmethylsulfonium perchlorate

A 8 g. (0.03 mole) quantity of p-anisylethylmethylsulfonium fluoroborate was converted to the perchlorate salt as previously described for the unsubstituted compound. The resulting white solid was recrystallized 2X from methanol/diethylether solutions and dried in vacuo.

Yield: 97%. m.p. 79-79.6°. N.m.r. ($CDCl_3$): τ8.63 (t,3H, J=7.5 c.p.s.), 6.67 (s,3H), ca. 6.08-6.50 (q,2H), 6.08 (s, 3H), 2.58-2.92 (m,2H), 1.83-2.17 (m,2H). Infrared (nujol): 585, 618, 1084, 1260, 1455, 2850, 2920, 2945 cm^{-1}.

Anal. Calcd. for $C_{10}H_{15}O_5SCl$: C, 42.47; H, 5.35

Found: C, 42.14, 42.17; H, 5.48, 5.68.

Optically active para-Anisylethylmethylsulfonium perchlorates

These were prepared by passage of the corresponding diastereoisomer of the resolved 2R,3R-dibenzoylhydrogen tartrate salt through the anion exchange resin, followed by neutralization of the eluent with methanolic perchloric acid, as described for the unsubstituted compound. The yields given are based on the amounts of resolved 2R,3R-dibenzoylhydrogen tartrate salt used.

Note: Drying the recrystallized salts in a Abderhalden pistol apparatus under refluxing acetone, or simply pumping in a vacuum dessicator, resulted in racemization of the optically active salts. It is thus recommended that the salts be air dried, or subjected to a vacuum dessicator for only short periods of time.

(+)-perchlorate

Yield: 90%. m.p. 79.6-80.2°. $[\alpha]_{365}^{25}$ + 19.5° (c 0.945, anhyd. methanol). N.m.r. ($CDCl_3$): τ8.63 (t,3H,J=7.5 c.p.s.), 6.67 (s,2H), ca. 6.08-6.50 (q,2H), 6.08 (s,3H), 1.83-2.92 (m,4H). Infrared (nujol): 585, 618, 1084, 1260, 1455, 2850, 2920, 2945 cm^{-1}.

Anal. Calcd. for $C_{10}H_{15}O_5SCl$: C, 42.47; H, 5.35.

Found: C, 42.73, 42.44; H, 5.58, 5.67.

Note: More of this compound was prepared at a later date m.p. 67.5-71.0°. $[\alpha]^{25}_{365}$ + 94.5°., demonstrating the variation of melting point with optical rotation.

(-)-perchlorate

Yield: 90%. m.p. 34-35°. $[\alpha]^{25}_{365}$ - 69.5° (c 0.922, anhyd. methanol). N.m.r. ($CDCl_3$): τ8.68 (t,3H,J=7.5 c.p.s.), 6.74 (s,3H), ca. 6.14-6.56 (q,2H), 6.14 (s,3H), 1.99-2.99 (m,4H). Infrared (nujol): superimposable with (+)-isomer.

Anal. Calcd. for $C_{10}H_{15}O_5SCl$: C, 42.47; H, 5.35.

Found: C, 42.21, 41.64; H, 5.34, 5.44.

para-Nitrothiophenol (sodium salt)

Prepared as described by Willgerodt (22) and Waldron and Reid (23). A 62% yield was obtained. No analysis was attempted.

para-Nitrophenyl ethyl sulfide

Prepared as described by Waldron and Reid (23). Yield: 52%. m.p. 40-41° (reported (24): 40°). N.m.r. ($CDCl_3$): τ8.67 (t,3H,J=7.5 c.p.s.), 6.73-7.18 (q,2H,J=7.5 c.p.s.), 2.57-2.86 (m,2H), 1.76-2.05 (m,2H). Infrared (KBr): 735, 848, 1082, 1330, 1502, 1570, 3440 cm^{-1}.

para-Nitrophenylethylmethylsulfonium fluoroborate

A 5 g. (0.027 mole) quantity of p-nitrophenyl ethyl sulfide was treated with 5 g. (0.034 mole) of trimethyloxonium fluoroborate in a flask fitted with a drying

tube, using methylene chloride as solvent. The reaction was complete in one hour. After work-up a pale yellow solid was obtained which was recrystallized 2X from methanol/diethylether solution.

Yield: 98%. m.p. 53-55°. N.m.r. (D_2O): τ8.69 (t,3H,J=7.5 c.p.s.), 6.70 (s,3H), 6.08-6.53 (q,2H), 1.40-1.96 (m,4H). Infrared (KBr): 728, 838, 1050, 1068, 1108, 1320, 1448, 3440 cm^{-1}.

<u>para-Nitrophenylethylmethylsulfonium 2R,3R-dibenzoylhydrogen tartrate</u>

A 4 g. (0.014 mole) quantity of p-nitrophenylethylmethylsulfonium fluoroborate was dissolved in a minimum amount of methanol and passed through the anion exchange resin. However, the whole procedure was carried out in a cold laboratory at -5°, since a previous attempt to carry out the exchange at 25°, resulted in a considerable amount of decomposition on the column. The eluent was allowed to drip into 5.3 g. (0.015 mole) of (-)-2R,3R-dibenzoyl tataric acid, dissolved in diethylether. It was observed that as the 2R,3R-dibenzoylhydrogen tartrate salt formed, it precipitated out of solution, indicating only a slight solubility in methanol. When exchange was complete the receiving flask contained a white solid suspended in a pale yellow solution having a nitrobenzene odour, indicating that even on the cooled column, some decomposition had occurred. The solid was filtered off and washed well with ether.

Yield: 77%. m.p. 117-119°. $[\alpha]_D^{25}$ - 70.4° (c 0.2698, anhyd. methanol). N.m.r. (dimethylsulfoxide-d_6): τ8.74-9.11 (t), 8.71 (s), 7.54 (s), 6.92 (s), 6.71 (s), 6.21-6.59 (q), 4.38 (s), 1.60-2.84 (m), 0.2 (s). A complicated spectrum was obtained, the peaks are not assigned. Infrared (KBr): 708, 1108, 1258, 1339, 1715, 3440 cm^{-1}.

The salt was resolved by dissolving 2 g. in 450 ml. of methanol and cooling the solution to 5°. No diethylether was added. After a 24 hour period, the crystals which had precipitated were filtered off. The crystals from the mother liquor were obtained by reducing the volume of methanol on a rotary evaporator, and then adding diethylether to the cloud point.

Racemic para-Nitrophenylethylmethylsulfonium perchlorate

A 5 g. (0.009 mole) quantity of unresolved p-nitrophenylethylmethylsulfonium 2R,3R-dibenzoylhydrogen tartrate salt was suspended in methanol and titrated with 5% methanolic perchloric acid. The perchlorate salt is very soluble in methanol, consequently, addition of the perchloric acid was terminated when the absence of a solid phase was observed. Diethylether was then added and a white solid precipitated out. The salt was filtered, washed with ether, and recrystallized 2X from methanol/ diethylether solution.

Yield: 93%. m.p. 49-51°. N.m.r. (dimethylsulfoxide-d_6): τ8.88 (t,3H), 6.71 (s,3H), 6.11-6.60 (q,2H), 1.40-1.99 (m,4H). Infrared (nujol): 1080, 1092, 1310, 1602, 3440 cm^{-1}.

Anal. Calcd. for $C_9H_{12}O_6SClN$: C, 36.30; H, 4.06; S, 10.77; N, 4.71.

Found: C, 36.02, 36.19; H, 4.09, 4.08; S, 10.82, 10.75; N, 4.81, 5.09.

(+)-para-Nitrophenylethylmethylsulfonium perchlorate

A 0.75 g. (0.0013 mole) quantity of the first crop of crystals obtained in the resolution of the 2R,3R-dibenzoylhydrogen tartrate salt was suspended in methanol, and titrated with 5% methanolic perchloric acid, as described for the racemic salt. After work-up, the initially formed oil solidified on scratching with a glass rod. The pale yellow solid was recrystallized 2X from methanol/diethylether solution.

Yield: 33%. m.p. 27.5-28.5°. $[\alpha]_{436}^{25}$ + 32.5° (c 0.9985, anhyd. methanol). N.m.r. (dimethylsulfoxide-d_6): τ8.82 (t,3H), 6.70 (s,3H), 6.04-6.53 (q,2H), 1.40-1.99 (m,4H). Infrared (KBr): 1090, 1120, 1340, 1530, 3440 cm^{-1}.

Anal. Calcd. for $C_9H_{12}O_6SClN$: C, 36.30; H, 4.06; S, 10.77; N, 4.71.

Found: C, 36.41, 36.60; H, 4.11, 4.20; S, 10.88, 10.86; N, 4.48, 4.53.

(-)-para-Nitrophenylethylmethylsulfonium perchlorate

A 1 g. (0.0017 mole) quantity of the crystals obtained from the mother liquor in the resolution of the 2R,3R-dibenzoylhydrogen tartrate salt was converted to the perchlorate salt as described for the (+)-isomer. After

work-up, the pale yellow solid was recrystallized 2X from methanol/diethylether solution.

Yield: 74%. m.p. 71.0-71.5°. $[\alpha]_{436}^{25}$ - 18.7° (c 1.211, anhyd. methanol). N.m.r. (dimethylsulfoxide-d_6): τ8.83 (t,3H), 6.71 (s,3H), 6.04-6.53 (q,2H), 1.40-1.93 (m,4H). Infrared (KBr): superimposable with the (+)-isomer.

Anal. Calcd. for $C_9H_{12}O_6SClN$: C, 36.30; H, 4.06; S, 10.77; N, 4.71.

Found: C, 36.28, 35.96; H, 3.97, 3.74; S, 10.78, 10.73; N, 4.70, 4.33.

Para-Hydroxyphenyl methyl sulfide

Prepared by the method of Suter and Hansen (20).

Yield: 63%. m.p. 81.5-82.0° (reported (20): 83-84°). N.m.r. ($CDCl_3$): τ7.60 (s,3H), 4.42 (s,1H), 2.58-3.36 (m,4H). Infrared (nujol): 538, 635, 820, 855, 1255, 1378, 1445, 1498, 2860, 2940, 3380 cm^{-1}.

para-Hydroxyphenylethylmethylsulfonium fluoroborate

A 5 g. (0.036 mole) quantity of p-hydroxyphenyl methyl sulfide was dissolved in diethylether in a 250 ml. flask fitted with a drying tube. A 7 g. (0.037 mole) quantity of triethyloxonium fluoroborate was added, and the flask flushed with nitrogen gas before replacing the drying tube. The reaction was complete in ca. 45 minutes, a white solid, insoluble in diethylether being formed. The solid was filtered and recrystallized from methanol/diethylether solution. It is noteworthy that in the reaction only

S-alkylation occurred, no O-alkylation was observed.

Yield: 87%. m.p. 109.6-111.6°. N.m.r. (dimethylsulfoxide-$\underline{d}_6$): τ8.79 (t,3H,J=7.5 c.p.s.), 6.75 (s,3H), 6.13-6.63 (q, 2H), 1.92-3.09 (m,4H). Infrared (nujol): 1280, 1425, 1438, 1452, 1500, 1583, 1600, 2850, 2930, 3390 cm^{-1}.

<u>para-Hydroxyphenylethylmethylsulfonium 2R,3R-dibenzoylhydrogen tartrate</u>

A 2 g. (0.008 mole) quantity of <u>p</u>-hydroxyphenylethylmethylsulfonium fluoroborate was dissolved in methanol and passed through the anion exchange resin in the usual manner. The eluent was neutralized with a solution of 2.8 g. (0.008 mole) of (-)-2R,3R-dibenzoyl tartaric acid dissolved in diethylether. After work-up a white solid was obtained.

Yield: 91%. m.p. 85-125°. $[\alpha]_D^{25}$ - 74.4° (<u>c</u> 0.3992, anhyd. methanol). N.m.r. (dimethylsulfoxide-$\underline{d}_6$): τ8.96 (t), 6.83 (s), 6.18-6.70 (q), 4.16 (s), 1.67-3.42 (m), 0.5 (s). Infrared (nujol): 715, 1110, 1260, 1375, 1450, 1712, 2850, 2920 cm^{-1}.

The salt was resolved by fractional crystallization from methanol/diethylether solution as described for the unsubstituted compound.

<u>Racemic para-Hydroxyphenylethylmethylsulfonium perchlorate</u>

A 2 g. (0.008 mole) quantity of <u>p</u>-hydroxyphenylethylmethylsulfonium fluoroborate was dissolved in methanol and passed through the anion exchange resin in the usual

way. The eluent was neutralized with a 5% methanolic solution of perchloric acid. After work-up a white solid was obtained which was recrystallized 2X from methanol/diethylether solution.

Yield: 100%. m.p. 129.6-130.6°. N.m.r. (dimethylsulfoxide-$\underline{d}_6$): τ8.90 (t,3H,J=7.5 c.p.s.), 6.85 (s,3H), 6.26-6.73 (q,2H), 2.84-3.18 (m,2H), 2.00-2.42 (m,2H), -0.5 (s,1H). Infrared (nujol): 840, 1050, 1110, 1455, 1582, 2860,2920, 3400 cm^{-1}.

Anal. Calcd. for $C_9H_{13}O_5SCl$: C, 40.22; H, 4.81; S, 11.93.
Found: C, 40.24, 40.08; H, 4.81, 4.92; S, 11.27, 11.40.

(+)-para-Hydroxyphenylethylmethylsulfonium perchlorate

A 2.5 g. (0.005 mole) quantity of the crystals obtained from the mother liquor in the resolution of the 2R,3R-dibenzoylhydrogen tartrate salt was converted to the perchlorate salt by passage through the anion exchange resin, and neutralization of the eluent with methanolic perchloric acid in the usual manner. After work-up the white solid was recrystallized 2X from methanol/diethylether solution.

Yield: 89%. m.p. 129.8-130.6°. $[\alpha]^{25}_{436}$ + 13.3° ($\underline{c}$ 0.9260, anhyd. methanol). N.m.r. (dimethylsulfoxide-$\underline{d}_6$): τ8.77 (t,3H,J=7.5 c.p.s.), 6.72 (s,3H), 6.13-6.62 (q,2H), 2.72-3.03 (m,2H), 1.93-2.26 (m,2H). Infrared (nujol): 840, 1060, 1105, 1280, 1500, 1585, 1600, 2860, 2920, 3300 cm^{-1}.

Anal. Calcd. for $C_9H_{13}O_5SCl$: C, 40.22; H, 4.88; S, 11.93.
Found: C, 39.97, 40.54; H, 4.45, 5.19; S, 11.18, 11.33.

(-)-para-Hydroxyphenylethylmethylsulfonium perchlorate

A 4 g. (0.007 mole) quantity of the first crop of crystals obtained in the resolution of the 2R,3R-dibenzoylhydrogen tartrate salt was converted to the perchlorate salt as described for the (+)-isomer. After work-up the white solid was recrystallized 2X from methanol/diethylether solution.

Yield: 94%. m.p. 129.8-130.6°. $[\alpha]_{436}^{25}$ - 31.2° (c 0.8680, anhyd. methanol). N.m.r. (dimethylsulfoxide-d_6): τ8.76 (t,3H,J=7.5 c.p.s.), 6.72 (s,3H), 6.12-6.62 (q,2H), 2.67-3.08 (m,2H), 1.98-2.28 (m,2H). Infrared (nujol): superimposable with the (+)-isomer.

Anal. Calcd. for $C_9H_{13}O_5SCl$: C, 40.22; H, 4.88; S, 11.93.

Found: C, 40.40, 40.73; H, 4.74, 4.53; S, 12.21, 12.00.

Note: Like the optically active p-anisylethylmethylsulfonium perchlorates, drying under vacuum resulted in loss of optical activity.

Dipolar species obtained from the para-Hydroxyphenylethylmethylsulfonium system

A 5 g. (0.02 mole) quantity of p-hydroxyphenylethylmethylsulfonium fluoroborate was dissolved in methanol and passed through the anion exchange resin in the usual manner. The eluent was collected in a flask surrounded by an ice/salt bath. When the exchange was complete, as indicated by a negative test for basicity with phenolphthalein indicator, the solvent was stripped off on a rotary evaporator.

A pale yellow oil remained, which solidified on pumping under vacuum. The off white solid was found to be very soluble in hydroxylic solvents such as water, methanol and ethanol, yielding basic solutions, but insoluble in all other solvents tried.

m.p. ca. 138-142 (opaque liquid) 142-143° (clear liquid). N.m.r. (D_2O): τ9.01 (t,3H,J=7.5 c.p.s.), 7.21 (s,3H), 6.59-7.09 (q,2H), 3.17-3.51 (m,2H), 2.51-2.84 (m,2H). Infrared (KBr): 840, 1070, 1120, 1380, 1485, 1500, 1580, 1595, 3040, 3450 cm^{-1}.

F^{19} (D_2O, $CFCl_3$ external standard): No fluorine resonance, indicating the absence of any fluoroborate anion as impurity.

Note: Passage of the sulfonium salt through the anion exchange resin will result in exchange of the fluoroborate anion for a hydroxide anion. This would then be expected to neutralize the phenolic proton, producing a dipolar species, plus a mole of water. A possible scheme is shown in Figure XI. Attempts were made to determine the exact structure of the compound, however the results were far from conclusive. The experiments performed are described below.

Experiment I. Treatment with fluoroboric acid

A 0.5 g. quantity of the compound was dissolved in methanol, and the resulting solution titrated with a 5% methanolic solution of fluoroboric acid. When the mixture was slightly acidic, diethylether was added, resulting in precipitation of a white solid. The solid was filtered

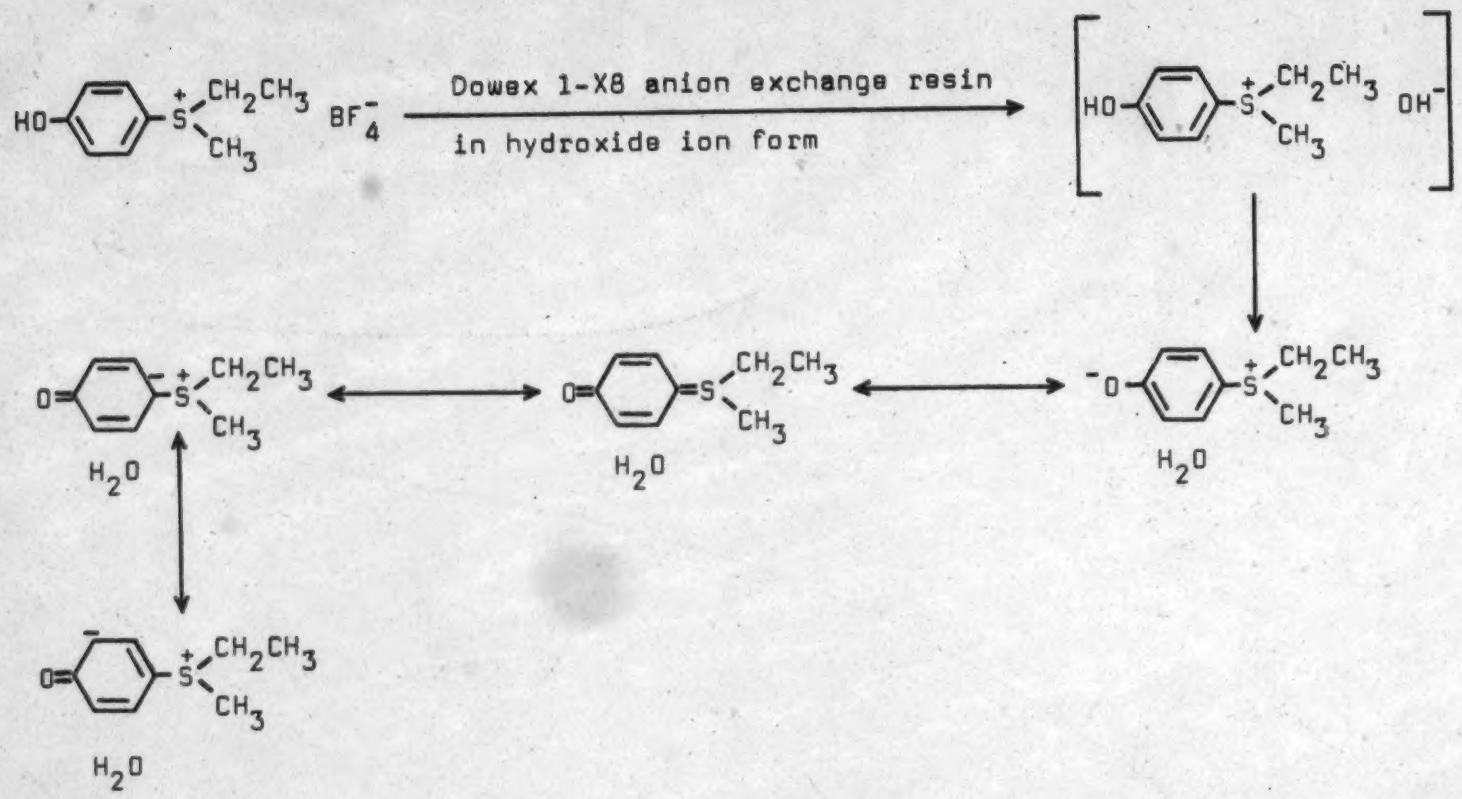
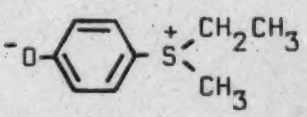


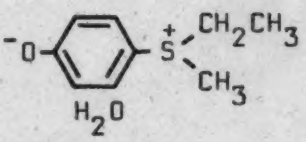
Figure XI. Dipolar species from para-Hydroxyphenylethylmethylsulfonium fluoroborate.

and recrystallized 2X from methanol/diethylether solution. Yield: 0.7 g. m.p. 110°. N.m.r. (D_2O): τ8.94 (t,3H,J=7.5 c.p.s.), 7.04 (s,3H), 6.42-6.92 (q,2H), 2.98-3.30 (q,2H), 2.26-2.62 (q,2H). Infrared (nujol): 1280, 1425, 1438, 1452, 1500, 1583, 1600, 2850, 2930, 3390 cm^{-1}.

Conclusion: The melting point, n.m.r. and i.r. spectra are identical with the p-hydroxyphenylethylmethylsulfonium fluoroborate salt. Hence, formation of the dipolar species is a reversible process.

Experiment II. Carbon, Hydrogen analyses

Calcd. for  : C, 64.25; H, 7.19.

Calcd. for  : C, 58.03; H, 7.53.

Found: C, 60.45, 59.97; H, 7.55, 7.38.

Conclusion: The analysis is more consistent with the structure containing a mole of water. Further possible evidence for the presence of water is a comparison of the impurity peaks in the n.m.r. spectrum, using D_2O as solvent. When run neat, the spectrum of D_2O shows an impurity peak at τ5.32 due to proton resonance. The n.m.r. spectrum of the proposed dipolar species in D_2O, shows a more intense peak at τ5.32, indicating the presence of water.

Experiment III. Drying in an Abderhalden pistol apparatus

A 0.58 g. quantity of the compound was placed

in a weighing boat, and subjected to a pressure of 1 mm., under refluxing acetone, in an Abderhalden pistol apparatus. Loss in weight and change in melting point were followed with time, the results are shown below.

Time (hr)	Loss in weight (g)	m.p.
24	0.015	ca. 139-143° (dec.)
48	0.020	ca. 134-142° (dec.)
140	0.100	ca. 118-130° (dec.)

The material obtained after 140 hr was pale yellow in color and slightly hygroscopic. The i.r. spectrum was identical with the starting material, however the carbon and hydrogen analyses had changed i.e. C, 62.98, 63.41; H, 7.13, 7.26.

Conclusion: The changes in mass and carbon and hydrogen analyses could indicate the removal of water from the compound.

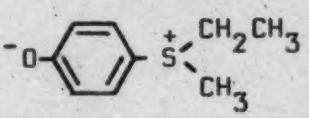
Experiment IV. Melting the compound

About 0.5 g. of the compound was weighed into a test tube and then placed in a Wood's metal bath, at a temperature of 136-140°. When all the material had melted, the pale yellow liquid was allowed to cool. Diethylether was then added, resulting in formation of a milky solution. On cooling to 5°, a white solid precipitated out, this was filtered off. N.m.r. and i.r. spectra showed it to be the proposed dipolar species. Removal of the diethylether from the filtrate yielded a yellow oil. This was shown to contain a mixture of sulfides, p-methoxyphenyl ethyl sulfide and

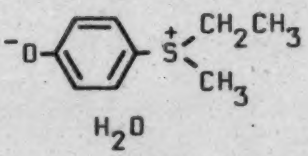
p-ethoxyphenyl methyl sulfide, presumably formed by trans-alkylations in the melt.

Conclusion: The experiment proved to be uninformative with regard to the structure of the dipolar species.

Experiment V. Molecular weight determination



M.W. = 168



M.W. = 186

Method A.

A known weight of the compound was dissolved in methanol, and 5 ml. aliquots titrated with standard hydrochloric acid, using bromophenyl blue as indicator. From the results, a value of 171.5 was calculated for the molecular weight.

Method B.

This was performed by the microanalyst using an ebullioscopic method. A value of 180 was obtained.

Conclusion: The discrepancy in the values is too great to form any definite opinion.

Experiment VI. Mass spectral analysis

Machine: MS-9. Direct probe. Starting temperature 120°. Major peaks: 196, 182, 168, 154, 140, 139, 125, 111, 97, 77, 69, 45 m.u.

Conclusion: The peak at 168 m.u. was strong, however no conclusive evidence can be drawn from the analysis.

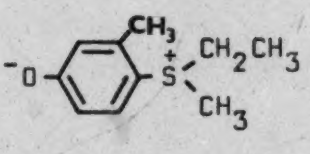
Experiment VII. Preparation of the dipolar species from ortho-Methyl-para-hydroxyphenylethylmethylsulfonium fluoroborate

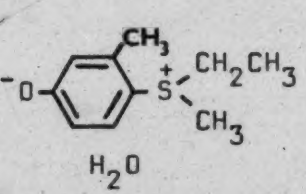
o-Methyl-p-hydroxyphenyl methyl sulfide (supplied by the Crown Zellerbach company), was converted to the sulfonium salt by treatment with triethyloxonium fluoroborate, using methylene chloride as solvent. The sulfonium salt had the following properties.

m.p. 124-125.5°. N.m.r. (D_2O): τ8.81 (t,3H), 7.62 (s,3H), 6.97 (s,3H), 6.36-6.82 (q,2H), 2.99-3.31 (m,2H), 2.29-2.54 (m,1H). Infrared (KBr): 1062, 1082, 1122, 1250, 1310, 1458, 1490, 1574, 1595, 1610, 3430 cm^{-1}.

The dipolar species was prepared by passage of a methanolic solution of the sulfonium salt through the anion exchange resin, as described for the p-hydroxyphenylethyl-methyl species. After work-up a white solid was obtained having the following properties.

m.p. 117.5-119.0°. N.m.r. (D_2O): τ8.97 (t,3H), 7.80 (s,3H), 7.19 (s,3H), 6.54-7.03 (q,2H), 3.24-3.66 (m,2H), 2.52-2.81 (m.1H). There was a large impurity peak at τ5.32 due to proton resonance of the solvent, and possible water in the compound. Infrared (nujol): 865, 1038, 1258, 1365, 1497, 1582, 3420 cm^{-1}.

Anal. Calcd. for  : C, 65.89; H, 7.74; S, 17.59.

Calcd. for  : C, 59.97; H, 8.05; S, 16.01.

Found: C, 58.94, 58.76; H, 7.95, 7.60; S, 16.21, 16.70.

Conclusion: This dipolar species was similar in all respects to the previous one, except for a cleaner melting point. Again, the n.m.r. spectrum and elemental analysis point to a structure containing a mole of water.

Preparation of the dipolar species in optically active form from optically active para-Hydroxyphenylethylmethylsulfonium perchlorate

A 1 g. (0.004 mole) quantity of p-hydroxyphenylethylmethylsulfonium perchlorate, $[\alpha]^{25}_{365}$ + 19.8° (c 0.9780, anhyd. methanol), was converted to the dipolar species as described for the racemic material. After work-up a white solid was obtained.

Yield: 0.6 g. m.p. ca. 138-141° (opaque liquid) ca. 141-143° (clear liquid). $[\alpha]^{25}_{365}$ + 38.0° (c 1.3830, anhyd. methanol). N.m.r. (D_2O): τ9.01 (t,3H,J=7.5 c.p.s.), 7.21 (s,3H), 6.59-7.09 (q,2H), 3.17-3.51 (m,2H), 2.51-2.84 (m,2H). Infrared (nujol): superimposable with the racemic material.

Note: After 10 half-lives of racemization in methanol at 50°

only racemic material was recovered, showing that no decomposition had taken place.

Isopropyl ethyl sulfide

Prepared by the method of M^{c}Allen et al. (25). b.p. 100-102^{o} at 700 mm. (reported (25): 107.3^{o} at 760 mm.) n_D^{25} 1.4376 (reported (25): 1.4382). N.m.r. (neat): τ8.58-9.00 (m,9H), 6.83-7.75 (m,3H). Infrared (neat): 545, 1150, 1238, 1360, 1380, 1450, 2870, 2930, 2960, 2970 cm^{-1}.

Isopropylethylmethylsulfonium iodide

A 10 g. (0.096 mole) quantity of isopropyl ethyl sulfide, together with 14.2 g. (0.10 mole) of methyl iodide were placed in a 125 ml. flask and kept in a dark cupboard for 20 hours. The product, a white solid, was recrystallized 2X from acetone/diethylether solution. Because of the compound's sensitivity to light, filtration and general handling were carried out in subdued lighting.

Yield: 61%. m.p. 150-155^{o} (sublimed). N.m.r. ($CDCl_3$): τ8.17-8.67 (m,9H), 6.77 (s,3H), 6.00-6.50 (q,2H), 5.43-5.92 (m,1H). Infrared (nujol): 552, 785, 1052, 1080, 1264, 1282, 1374, 1408, 1422, 1458, 2860, 2950 cm^{-1}.

Isopropylethylmethylsulfonium 2R,3R-dibenzoylhydrogen tartrate

Prepared by the passage of a methanolic solution of isopropylethylmethylsulfonium iodide through the anion exchange resin in the usual manner, and neutralization of the eluent with 2R,3R-dibenzoyl tartaric acid.

Yield: 85%. m.p. 120-121.5°. $[\alpha]_D^{25}$ - 97.6° (c 0.4496, anhyd. methanol). N.m.r. (dimethylsulfoxide-d_6): τ8.72-9.18 (m,9H), 7.42 (s,3H), 6.26-7.19 (m,3H), 4.88 (s,2H), 2.00-2.93 (m,10H). Infrared (nujol): 558, 715, 1105, 1260, 1372, 1455, 1700, 2900 cm^{-1}.

Resolution by fractional crystallization from methanol/diethylether solution was found to be difficult, only one of the isomers being isolated.

(-)-Isopropylethylmethylsulfonium perchlorate

The first crop of crystals obtained in the resolution of the 2R,3R-dibenzoylhydrogen tartrate salt, was dissolved in methanol, and converted to the perchlorate salt by passage through the anion exchange resin, and neutralization of the eluent with methanolic perchloric acid, in the usual manner. After work-up a white "tacky" solid was obtained. Repeated recrystallization from methanol/diethylether solutions failed to yield a crystalline material.

m.p. 155-160°. $[\alpha]_{365}^{25}$ - 10.6° (c 0.8240, anhyd. methanol). N.m.r. (dimethylsulfoxide-d_6): τ8.42-8.83 (m,9H), 7.20 (s, 3H), 6.03-6.97 (m,3H). Infrared (nujol): 618, 770, 780, 920, 1090, 1255, 1370, 1430, 1460, 2940, 2980, 3020, 3620 cm^{-1}.
Anal. Calcd.for $C_6H_{15}O_4SCl$: C, 32.95; H, 6.91.

Found: C, 32.00, 31.88; H, 6.46, 6.65.

Note: Several other salts were prepared in an attempt to obtain a crystalline material i.e. fluoroborate, perfluoromethanesulfonate, p-nitrobenzoate, 3,5-dinitrobenzoate and bromide, all without success.

Cyclohexyl bromide

Prepared as described by Vogel (26).

N.m.r. (neat): τ7.46-8.82 (m,10H), 5.41-5.93 (m,1H).

Cyclohexyl xanthate ester

Prepared as described by Borsche and Lange (27).

Yield: 20%. b.p. 126-128° at 11 mm. (reported (27): 150-153° at 16 mm.). N.m.r. ($CDCl_3$): τ7.82-8.88 (m,13H), 6.16-6.66 (m,1H), 5.19-5.64 (m,2H). Infrared (neat): 810, 880, 990, 1200, 1255, 1440, 2840, 2920 cm^{-1}.

Cyclohexyl mercaptan

The method of Borsche and Lange (28) involved the use of gaseous ammonia to split the cyclohexyl xanthate ester. However, several attempts to repeat their experiment failed. It was found that using a 2:1 mole ratio of ethanolic potassium hydroxide to ester, refluxing for 2-4 hours, adding dilute hydrochloric acid to neutralize the excess base and liberate the free mercaptan, followed by extraction with diethylether, resulted in a good yield of mercaptan.

Yield: 90%. b.p. 41-43° at 12 mm. (reported (28): 158-160° at 760 mm.). N.m.r. ($CDCl_3$): τ7.78-8.98 (m,10H), 6.98-7.56 (m,1H). Infrared (neat): 880, 990, 1195, 1255, 1440, 2840, 2920 cm^{-1}.

Cyclohexyl ethyl sulfide

Prepared as described by Borsche and Lange (29).

Yield: 60%. b.p. 70-73° at 10 mm. (reported (30): 68-70°

at 10 mm.). n_D^{25} 1.4823 (reported (30): n_D^{20} 1.4908). N.m.r. ($CDCl_3$): τ7.84-7.95 (m,13H), 7.23-7.69 (m,3H).

Cyclohexylethylmethylsulfonium fluoroborate

A 6 g. (0.042 mole) quantity of cyclohexyl ethyl sulfide was dissolved in 30 ml. of methylene chloride in a flask fitted with a drying tube. The flask was flushed with nitrogen gas and 7 g. (0.048 mole) of trimethyloxonium fluoroborate were added. Reaction was rapid and complete within approximately 45 minutes. Addition of diethylether resulted in formation of an oil, all attempts to obtain a crystalline solid were unsuccessful.

Yield: 95%. N.m.r. ($CDCl_3$): τ7.61-8.66 (m,16H), 7.13 (s, 3H), 6.36-6.86 (m,3H). Infrared (nujol): 1050, 1268, 1450, 2860, 2940 cm^{-1}.

Cyclohexylethylmethylsulfonium α-bromo-π-camphorsulfonate

Although the 2R,3R-dibenzoylhydrogen tartrate salt was a solid, melting at 125°, no resolution could be effected after repeated attempts. Similarly, attempts to resolve the tartrate and camphorsulfonate salts were unsuccessful. Resolution was finally achieved using the α-bromo-π-camphorsulfonate salt. The resolving agent comes in the form of it's ammonium salt. A methanolic solution of the free acid was prepared by passage of the ammonium salt through a cation exchange resin in hydrogen ion form. The cyclohexylethylmethylsulfonium fluoroborate salt was converted to the hydroxide by passage through the anion

exchange resin in the usual manner. The eluent was then neutralized to a pH of ca. 8 with the methanolic solution of α-bromo-π-camphorsulfonic acid. The bulk of the solvent was removed on a rotary evaporator and diethylether added to precipitate the salt. The initially formed oil gave a white solid on crystallization from acetone/diethylether solution.

Yield: 80%. m.p. 75-76°. $[\alpha]_D^{25}$ + 61.9° (c 0.4300, anhyd. methanol). N.m.r. ($CDCl_3$): very complicated spectrum obtained. Infrared (KBr): 1030, 1170, 1445, 1730, 2930, 3415 cm^{-1}.

No separation was achieved from methanol/diethylether solution. The salt was resolved by fractional crystallization from acetone. A quantity of the salt was dissolved in a minimum amount of acetone, cooled to 5°, and left overnight. The mother liquor was decanted and the remaining crystals collected and washed well with diethylether. Addition of diethylether to the mother liquor yielded the other diasteroisomer.

(+)-Cyclohexylethylmethylsulfonium perchlorate

This was prepared by passage of the first crop of crystals from the resolution of the α-bromo-π-camphorsulfonate salt through the anion exchange resin in the usual manner. After work-up an oil was obtained, all attempts to obtain a solid material were unsuccessful.

$[\alpha]_{365}^{25}$ + 17.4° (c 1.273, anhyd. methanol). N.m.r. ($CDCl_3$): τ7.60-8.77 (m,13H), 7.09 (s,3H), 6.35-6.82 (m,3H). Infrared (neat): 750, 1085, 1450, 2940 cm^{-1}.

(-)-Cyclohexylethylmethylsulfonium perchlorate

The crystals obtained from the mother liquor in the resolution of the α-bromo-π-camphorsulfonate salt were converted to the perchlorate salt as described for the (+)-isomer. After work-up an oil was obtained, attempts to obtain a solid material were unsuccessful.

$[\alpha]_{365}^{25}$ - 4.7° (c 1.119, anhyd. methanol). N.m.r. ($CDCl_3$): τ7.62-8.62 (m,13H), 7.07 (s,3H), 6.32-6.78 (m,3H). Infrared (neat): superimposable with the (+)-isomer.

KINETICS

TITRIMETRIC RATES

Note: The following method does not apply to the p-hydroxyphenylethylmethyl system.

The sulfonium salt was accurately weighed in a tared volumetric flask. Enough solvent to dissolve the salt, together with as many aliquots of a standard solution of 2,6-lutidine as required, was added to the flask. After dilution to the mark, the solution was equilibrated by shaking the flask 100 times.

For the reactions the sealed ampoule technique was employed. Aliquots of the solution (5.3 ml.), were transfered to partially drawn out test tubes which had previously soaked overnight in a hot soap solution, rinsed 8 times with distilled water and dried overnight in an oven at 120°. The tubes were sealed and placed in a constant temperature bath, 50.00±0.02, 70.00±0.02, or 90.00±0.02°. At appropriate time intervals the ampoules were removed from the bath, placed in an ice-acetone bath and shaken for 30 seconds in order to quench the reaction. The first point was taken at least four minutes after the ampoules were placed in the bath so as to ensure temperature equilibration. Infinity measurements were taken at approximately 10 and 20 half-lives. Before the ampoules were broken open, they were allowed to equilibrate to 25° in a constant temperature bath for five minutes.

A 5 ml. aliquot was removed by means of a calibrated automatic pipette and delivered into a 50 ml. Erlenmeyer flask containing 25 ml. of boiled distilled water. Each sample was titrated for developing acid with a standard solution of sodium methoxide using phenolphthalein as indicator.

The rate constants calculated are based on the experimental infinity values, usually 100±3%, thus measuring the total rate of reaction. The rates were followed to about 85% completion. Percentage infinity values were obtained from the following relationship:

$$\% \text{ infinity titer} = \frac{V_{\infty} - V_B}{\text{Theoretical infinity titer}} \times 100$$

where V_{∞} is the experimental infinity titer and V_B is the average titer of the blanks. The blanks consisted of an equal amount of solvent containing inert salt and/or base, but not the reacting substrate.

SOLVOLYSIS OF p-HYDROXYPHENYLETHYLMETHYLSULFONIUM PERCHLORATE

This was followed using ultra-violet spectroscopy by observing the decrease in the concentration of the unreacted sulfonium salt, converted to its phenoxide ion form, at appropriate time intervals. Solvolysis results in the formation of p-hydroxyphenyl methyl sulfide, the phenoxide ion form of which could absorb in the region of absorbance of the salt. Ultra-violet data has already been given on the salt (Table XI), the absorbance due to the phenoxide ion form occurring at

279-280 mμ. Table XIV gives the data for p-hydroxyphenyl methyl sulfide. The results indicate that the absorbances for both the phenol and phenoxide forms of the sulfide occur approximately in the same position ca. 260 mμ. It was decided that the solvolysis reaction could be conveniently followed by taking aliquots of the reaction solution at appropriate time intervals, adding base to convert all the phenol (from the formed sulfide and unreacted salt) to phenoxide ion, then after dilution to the required concentration, observing the decrease in absorbance due to the unreacted salt (279 mμ). To test the proposed method, a synthetic mixture was prepared, corresponding to ca. 50% reaction:

$$[\text{Salt}] = 4.28\times10^{-5}$$

$$[\text{Sulfide}] = 5.00\times10^{-5}$$

$$[\text{NaOCH}_3] = 4.88\times10^{-3}$$

From the spectrum λ_{max} had moved to 270 mμ, however, from the absorbance at 279 mμ an estimate of the concentration of the salt could be made, which was then compared with the experimental value.

Result:

$$A_{279m\mu} = 0.80 \quad \varepsilon = 18{,}000 \text{ (from previous work)}$$

$$\therefore C = \frac{0.8}{18{,}000} = 4.4\times10^{-5}$$

This value compares well with the synthetic composition. The exact method for the solvolysis rate run is given below:

Method:

A known weight of the salt was dissolved in anhyd-

TABLE XIV

U.V. DATA ON *P*-HYDROXYPHENYL METHYL SULFIDE IN ANHYDROUS METHANOL

[Sulfide] ($X10^{-4}$)	[$HClO_4$] ($X10^{-4}$)	[$NaOCH_3$] ($X10^{-4}$)	OBSERVATIONS
2.00	—	—	major peak at 260 mμ
1.43	—	1.44	major peak at 260 mμ
2.00	—	97.6	broad bond at *ca.* 260 mμ
2.00	488.0	—	major peak at 258 mμ

rous methanol (with or without added 2,6-lutidine) in a volumetric flask. After mixing, 3 ml. aliquots of the solution were placed in partially drawn out, clean test tubes. The tubes were sealed and placed in a constant temperature oil bath at 90.00±0.02°. Twelve minutes were allowed for equilibration after which time one tube was pulled as a blank. The tube was cracked open, and 1 ml. of the solution was diluted to 250 ml. with reagent methanol containing 5 ml. of 0.244M sodium methoxide. After mixing thoroughly the spectrum was obtained. Other tubes were pulled at appropriate time intervals. The results are shown in Tables III and IV.

POLARIMETRIC RATES

Method I

Aliquots of a standard solution of the optically active sulfonium salt were transferred to ampoules. The ampoules were sealed and placed in a constant temperature bath as described for the titrimetric rate analyses. Reactions measured above 25° were quenched as previously described. After equilibration to 25°, the ampoules were broken open and an aliquot of the solution was transferred to a 1 dm. polarimeter tube. The optical rotation was obtained from the digital readout of a model 141 Perkin-Elmer Polarimeter. Measurements were made using an incident light beam having a wavelength of 436 mμ or 365 mμ. A "zero" reading was obtained before and after each measurement.

Method II

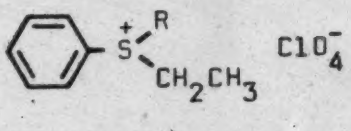
Water from a constant temperature bath, 50.00±0.02 or 25.00±0.02°, was circulated through jacketed polarimeter tubes. An aliquot of the solution of the optically active salt was placed in the polarimeter tube and the optical rotation was measured at appropriate time intervals. Where the rates were not excessively fast, a "zero" reading was taken before and after each run. The rate constants were calculated on the basis of the experimental infinity obtained after 10 half-lives (zero).

CHAPTER II

INTRODUCTION OF LARGER GROUPS - AN INVESTIGATION OF STERIC EFFECTS UPON THE RATE OF INVERSION

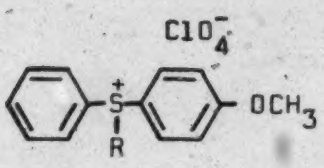
Kincaid and Henriques (31) suggested in 1940 that steric effects could alter the rates of pyramidal inversion reactions. They suggested that as substituents were made larger, the non-bonded interactions in the ground state would make the molecule more nearly planar, and hence reduce the activation energy to inversion.

This chapter describes the effect on the inversion rate of replacing the methyl group in the phenylethylmethyl system by larger primary groups, and the effect of replacing the methyl and ethyl groups respectively, by a phenyl group, in the p-anisylethylmethyl system. The solvolysis and racemization rates of the following compounds were studied.



VIII, R = $CH_3(CH_2)_2$

IX, R = $CH_3(CH_2)_3$



X, R = CH_3

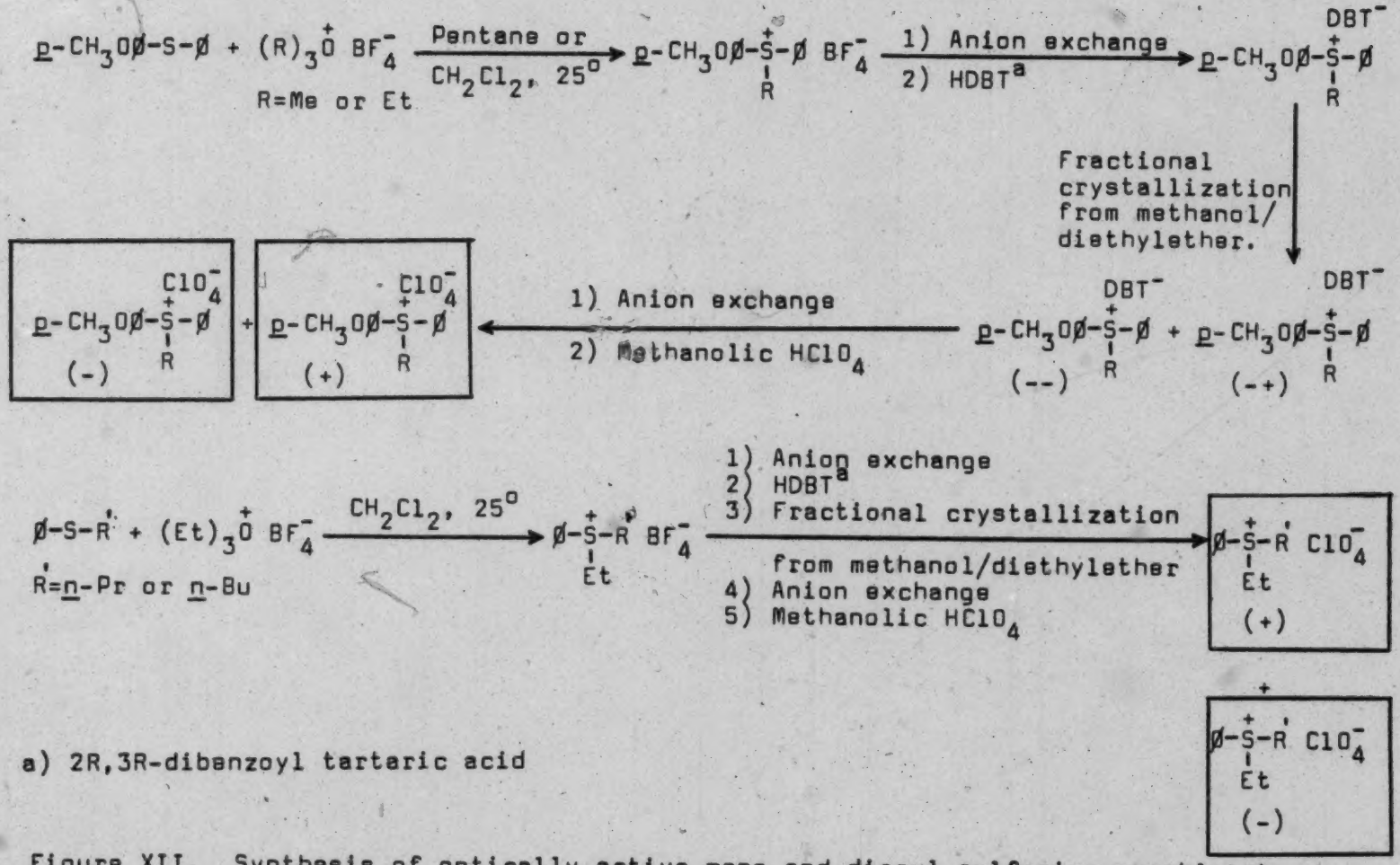
XI, R = CH_3CH_2

The results obtained give the first good evidence for steric effects upon the inversion of an acyclic pyramidal system. Attempts to prepare acyclic optically active triaryl sulfonium salts were unsuccessful, however, using the results from the mono and diaryl systems, an estimate can be made for the half-life for racemization of the triaryl sulfonium salt system.

SYNTHESIS AND RESOLUTION

The fluoroborate salts were prepared by reaction of the appropriate sulfide with Meerwein's Reagent (17). Conversion to the 2R,3R-dibenzoylhydrogen tartrate salt was accomplished by passage of a methanolic solution of the fluoroborate salt through a Dowex 1-X8 anion exchange column in hydroxide ion form, followed by neutralization of the eluent with (-)-2R,3R-dibenzoyl tartaric acid. Resolution was effected by fractional crystallization of the 2R,3R-dibenzoylhydrogen tartrate salts from methanol/diethylether solutions. After separation of the diastereoisomers, the optically active perchlorates were prepared by passage through the anion exchange column, followed by neutralization of the eluent with a 5% methanolic solution of perchloric acid. The scheme is outlined in Figure XII.

All compounds gave satisfactory elemental analyses. These, together with n.m.r. and i.r. spectra and melting points are reported with the detailed synthetic procedures



a) 2R,3R-dibenzoyl tartaric acid

Figure XII. Synthesis of optically active mono and diaryl sulfonium perchlorates.

in the experimental section.

SOLVOLYSIS STUDIES

The same method as used for the arylethylmethylsulfonium systems was employed, that is, following the rate of appearance of acid in the methanolysis of the perchlorate salts.

The titrimetric rate constants, k_t, were calculated from the relationship

$$k_t = 2.303 \log \frac{V_\infty - V_0}{V_\infty - V_t} .$$

Reactions were usually followed to about 85% completion, and good straight lines were obtained when log $(V_\infty - V_t)$ was plotted against time. Typical titrimetric rate analyses are shown in Tables XV and XVI; Figures XIII and XIV illustrate the corresponding kinetic plots. Table XVII shows the complete solvolysis rate data for the systems studied.

RACEMIZATION STUDIES

The same methods as used for the arylethylmethylsulfonium systems were employed. The first order rate constants were calculated from the relationship

$$k_\alpha = 2.303 \log \frac{\alpha_\infty - \alpha_0}{\alpha_\infty - \alpha_t} .$$

Reactions were usually followed to about 85% completion, and good straight lines were obtained when log $(\alpha_\infty - \alpha_t)$ was plotted against time. Typical racemization rate analyses are shown in Tables XVIII and XIX; Figures XV and XVI illustrate the corresponding kinetic plots. Table XX shows the complete racemization rate data for the systems studied.

TABLE XV

METHANOLYSIS OF RACEMIC P-ANISYLPHENYLMETHYLSULFONIUM PERCHLORATE IN THE PRESENCE OF 2,6-LUTIDINE AT 90.00±0.02°

[SALT] : 0.01594; [2,6-LUTIDINE] : 0.03702.

Aliquot: 5.00 ml; Titrant: $NaOCH_3$, 0.0365M.

Indicator: Phenolphthalein.

Theoretical infinity titer: 2.207 ml.

Experimental infinity titer: 2.034 ml.

TIME ($X10^3$ sec)	TITER (ml.)	log $(V_\infty - V_t)$	$10^5 k_t$ (sec^{-1})
0	0.083	0.3120	—
4.50	0.289	0.2417	2.48
7.20	0.429	0.2054	2.71
11.70	0.613	0.1526	2.70
14.40	0.708	0.1225	2.68
18.00	0.803	0.0902	2.55
23.40	0.997	0.1570	2.69
27.90	1.102	$\bar{1}$.9694	2.64
34.62	1.237	$\bar{1}$.9015	2.57
39.60	1.316	$\bar{1}$.8561	2.51
48.30	1.496	$\bar{1}$.7308	2.66
85.50	1.805	$\bar{1}$.3597	2.48
		AVERAGE:	2.61 ± 0.08

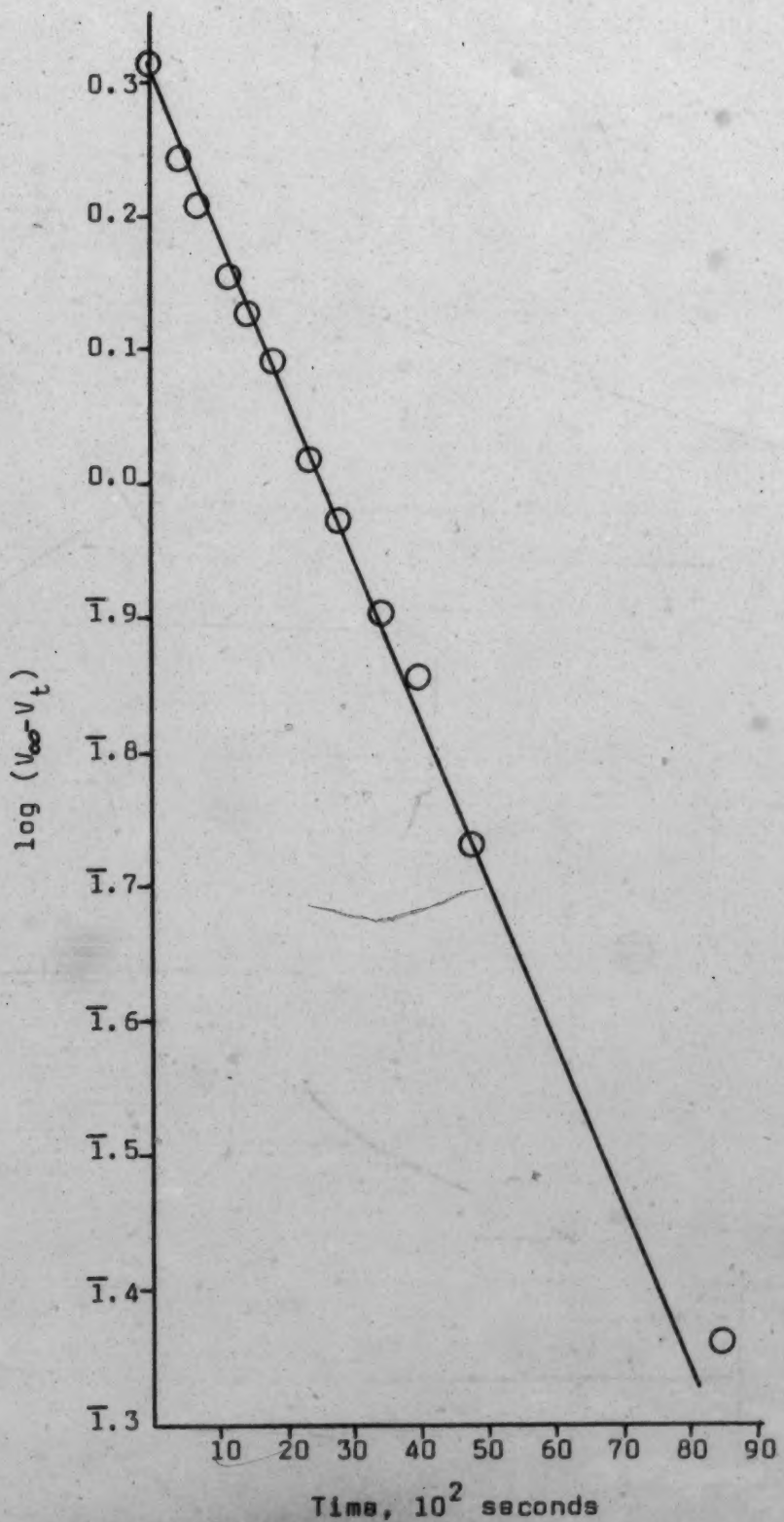


Figure XIII. Methanolysis of racemic p-Anisylethylmethylsulfonium perchlorate in the presence of 2,6-Lutidine at 90.00°.

TABLE XVI

METHANOLYSIS OF RACEMIC PHENYL-n-PROPYLETHYLSULFONIUM PERCHLORATE IN THE PRESENCE OF 2,6-LUTIDINE AT 90.00±0.02°

[SALT]: 0.02412; [2,6-LUTIDINE]: 0.06137.

Aliquot: 5.00ml; Titrant: $NaOCH_3$, 0.0365M.

Indicator: Phenolphthalein.

Theoretical infinity titer: 3.398 ml.

Experimental infinity titer: 3.316 ml.

TIME ($X10^4$ sec)	TITER (ml.)	$\log (V_\infty - V_t)$	$10^6 k_t$ (sec^{-1})
0	0.040	0.5149	—
2.67	0.648	0.4262	7.69
3.94	0.858	0.3906	4.29
4.65	1.047	0.3558	7.90
5.43	1.177	0.3302	7.85
6.69	1.346	0.2945	7.60
7.62	1.536	0.2504	8.01
8.64	1.626	0.2279	7.66
11.13	1.955	0.1339	7.89
13.65	2.174	0.0577	7.72
16.74	2.463	$\bar{1}$.9309	8.04
21.99	2.703	$\bar{1}$.7875	7.62
		AVERAGE:	7.75 ± 0.17

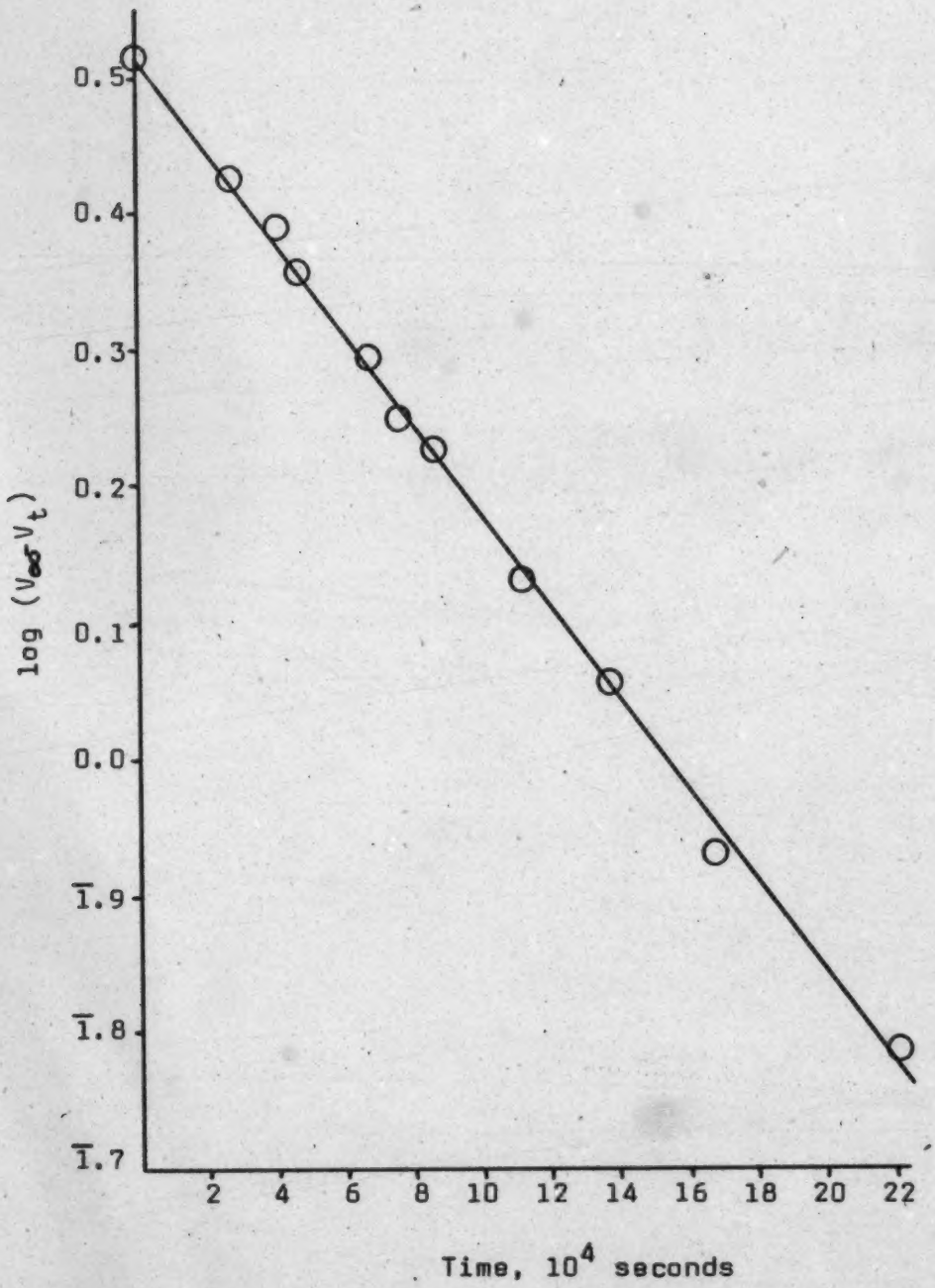


Figure XIV. Methanolysis of racemic Phenyl-n-propyl-ethylsulfonium perchlorate in the presence of 2,6-Lutidine at 90.00°.

TABLE XVII

SOLVOLYSIS OF RACEMIC MONOARYLDIALKYL AND DIARYLALKYLSULFONIUM PERCHLORATES IN ANHYDROUS METHANOL IN THE PRESENCE OF 2,6-LUTIDINE

SYSTEM[a]	TEMP	[SALT]	[2,6-LUTIDINE]	$10^5 k_t$ (sec^{-1})
p-Anisylphenylmethyl	90	0.0159	0.0370	2.61 ± 0.08
p-Anisylphenylethyl	90	0.0214	0.0534	6.21 ± 0.27
p-Anisylphenylethyl	50	0.0216	0.0582	0.0957 ± 0.0039
Phenyl-n-propylethyl	90	0.0241	0.0614	0.757 ± 0.017
Phenyl-n-butylethyl	90	0.0228	0.0571	0.561 ± 0.015

a) Phenylethylmethyl $10^5 k_t^{90}$ = 0.651 ± 0.002

TABLE XVIII

RACEMIZATION OF (+)-P-ANISYLPHENYLETHYLSULFONIUM PERCHLORATE IN ANHYDROUS METHANOL AT 50.00°

METHOD II [SALT] : 0.02952

TIME ($X10^2$ sec)	$\alpha^{50}_{365m\mu}$	log $(\alpha_\infty - \alpha_t)$	$10^3 k\alpha$ (sec^{-1})
0	+0.306	$\bar{1}$.4857	—
0.6	+0.271	$\bar{1}$.4330	2.03
1.20	+0.240	$\bar{1}$.3802	2.02
1.80	+0.212	$\bar{1}$.3263	2.04
2.40	+0.188	$\bar{1}$.2742	2.03
3.00	+0.165	$\bar{1}$.2175	2.06
3.60	+0.146	$\bar{1}$.1644	2.06
4.20	+0.130	$\bar{1}$.1139	2.04
4.80	+0.115	$\bar{1}$.0607	2.04
5.40	+0.101	$\bar{1}$.0043	2.05
6.00	+0.091	$\bar{2}$.9590	2.02
6.60	+0.080	$\bar{2}$.9031	2.03
7.20	+0.070	$\bar{2}$.8451	2.05
7.80	+0.063	$\bar{2}$.7993	2.03
8.40	+0.056	$\bar{2}$.7482	2.02
9.00	+0.049	$\bar{2}$.6902	2.04
10.20	+0.038	$\bar{2}$.5798	2.05
11.40	+0.029	$\bar{2}$.4624	2.07
12.60	+0.024	$\bar{2}$.3802	2.05
16.20	+0.012	$\bar{2}$.0792	2.00
720.00	0.000	—	—

AVERAGE: 2.04 ± 0.013

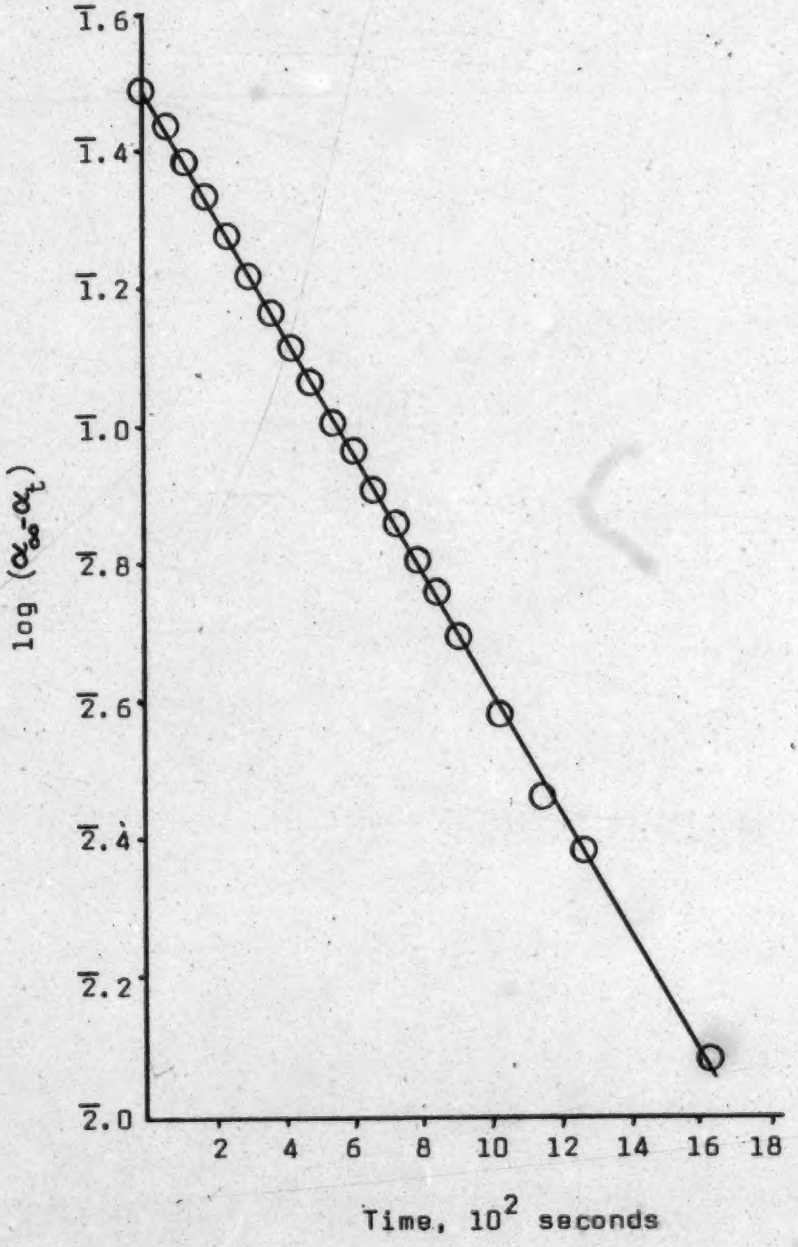


Figure XV. Racemization of (+)-p-Anisylphenylethylsulfonium perchlorate in anhydrous methanol at 50.00° (Method II).

TABLE XIX

RACEMIZATION OF (-)-PHENYL-n-PROPYLETHYLSULFONIUM PERCHLORATE IN ANHYDROUS METHANOL AT 50.00°

METHOD II [SALT] : 0.04071

TIME ($X10^2$ sec)	$\alpha^{50}_{365m\mu}$	log $(\alpha_\infty - \alpha_t)$	$10^4 k_\alpha$ (sec^{-1})
0	-0.128	$\bar{1}.1072$	—
3.0	-0.115	$\bar{1}.0607$	3.57
6.0	-0.103	$\bar{1}.0128$	3.62
9.0	-0.095	$\bar{2}.9777$	3.31
12.0	-0.087	$\bar{2}.9395$	3.22
15.0	-0.078	$\bar{2}.8921$	3.30
18.0	-0.071	$\bar{2}.8513$	3.27
21.0	-0.063	$\bar{2}.7993$	3.38
24.0	-0.059	$\bar{2}.7709$	3.23
30.0	-0.047	$\bar{2}.6721$	3.34
36.0	-0.040	$\bar{2}.6201$	3.23
42.6	-0.033	$\bar{2}.5185$	3.18
52.2	-0.023	$\bar{2}.3617$	3.29
1800.0	0.000	—	—
		AVERAGE:	3.33 ± 0.10

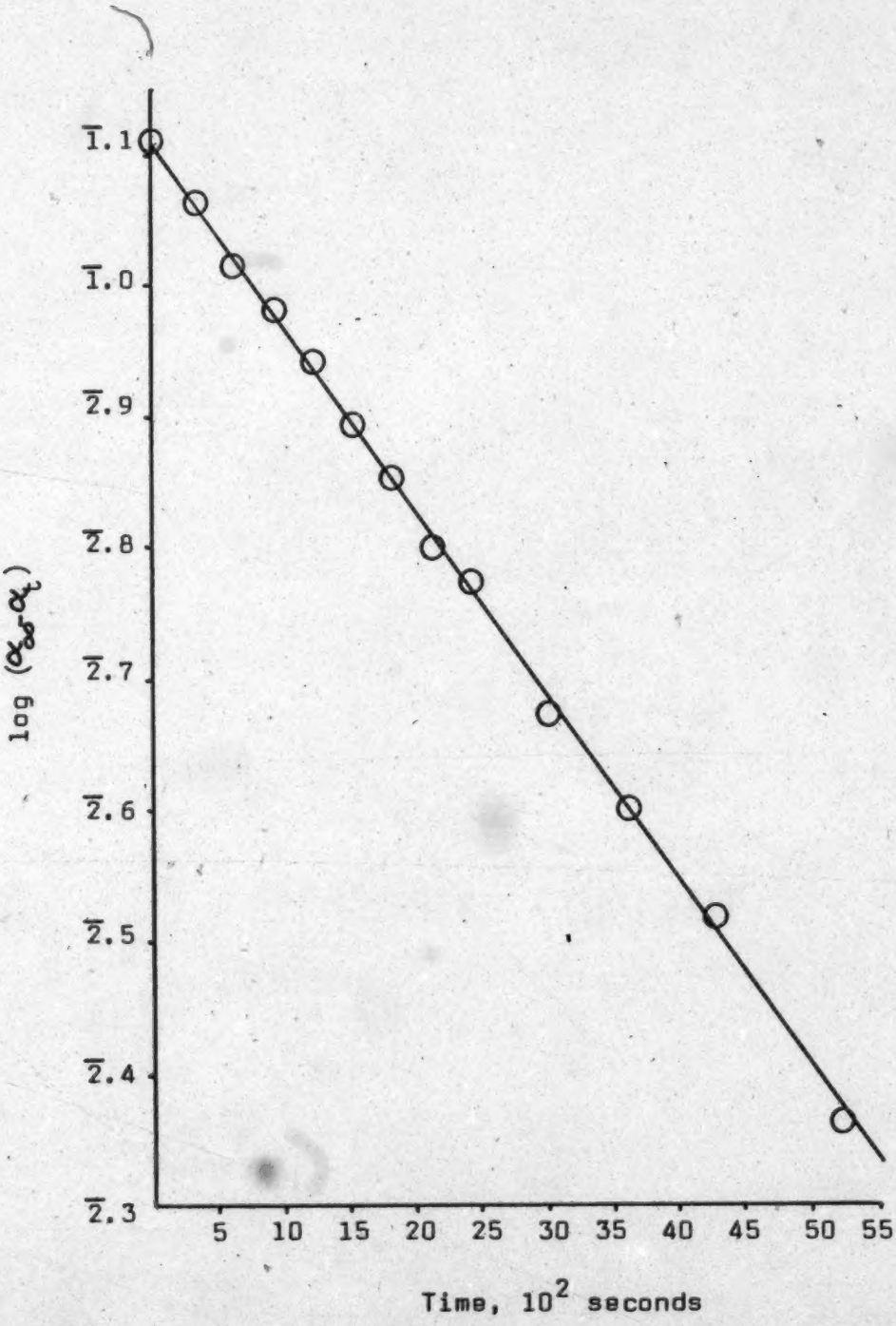


Figure XVI. Racemization of (-)-Phenyl-n-propylethylsulfonium perchlorate in anhydrous methanol at 50.00° (Method II).

TABLE XX

RACEMIZATION OF MONOARYLDIALKYL AND DIARYLALKYLSULFONIUM PERCHLORATES IN ANHYDROUS METHANOL

SYSTEM[a]	TEMP	ISOMER	[SALT]	$10^5 k_\alpha$ (sec^{-1})
p-Anisylphenylmethyl	25	+	0.0300	1.05 ± 0.05
p-Anisylphenylmethyl	50	+	0.0296	29.6 ± 0.8
p-Anisylphenylmethyl	50	-	0.0354	28.3 ± 0.9
p-Anisylphenylethyl	25	+	0.0303	8.27 ± 0.12
p-Anisylphenylethyl	25	-	0.0312	8.54 ± 0.89
p-Anisylphenylethyl	50	+	0.0295	204.0 ± 1.0
p-Anisylphenylethyl	50	-	0.0604	203.0 ± 7.0
Phenyl-n-propylethyl	25	+	0.0370	1.06 ± 0.03
Phenyl-n-propylethyl	50	+	0.0363	32.2 ± 0.4
Phenyl-n-propylethyl	50	-	0.0407	33.3 ± 1.0
Phenyl-n-butylethyl	25	+	0.0372	0.827 ± 0.018
Phenyl-n-butylethyl	50	+	0.0387	27.4 ± 0.5
Phenyl-n-butylethyl	50	-	0.0440	27.3 ± 0.9

a) Phenylethylmethyl $10^5 k_\alpha^{50} = 2.94 \pm 0.06$

DISCUSSION

In Chapter I it was shown that electronic effects played no significant part in the racemization of arylethylmethylsulfonium perchlorates via a pyramidal inversion mechanism. The results obtained for the monoaryldialkyl and diarylmonoalkyl systems given in this chapter indicate that steric effects have a profound effect on the inversion process.

A comparison of the solvolysis and racemization rate constants for VIII, IX, X and XI shows that solvolysis does not play any significant role in the racemization process and the assumption can be made that:

LOSS OF OPTICAL ACTIVITY = k_{α}.

The relative methanolysis rate constants, k_t, at 90.00° for I : VIII : IX are 1 : 1.3 : 1.0. The relative racemization rate constants, k_{α}, in methanol at 50.00° for I : VIII : IX are 1 : 11.0 : 9.3, and in methanol at 25.00° are 1 : 14.3 : 11.2.

The relative methanolysis rate constants, k_t, at 90.00° for I : X : XI are 1 : 4.4 : 10.6. The relative racemization rate constants, k_{α}, in methanol at 50.00° for I : X : XI are 1 : 10.7 : 69.4, and in methanol at 25.00° are 1 : 14.2 : 111.8. Replacement of the ethyl group in the p-anisylethylmethylsulfonium system by a phenyl group results in a rate increase of ca. 10 (at 50.00°), replacement of the

methyl group in the same system by a phenyl group, results in a rate increase of *ca.* 70 (at 50.00°). These results are readily explained in terms of steric effects. The presence of bulky substituents leads to appreciable non-bonded repulsions which are stronger in the pyramidal than in the planar state, where repulsions are partially relieved. As a consequence, the pyramidal state is destabilized with respect to the transition state, and the inversion barrier would be expected to decrease.

A similar effect is observed when the methyl group of the phenylethylmethyl system is replaced by a larger primary alkyl group (*n*-propyl or *n*-butyl). Again, an increase in rate of *ca.* 10 (at 50.00°) is observed. This large increase in the racemization rate is surprising, however, it is difficult to rationalize on anything but steric grounds. Increasing the chain length of the alkyl group does not increase the racemization rate, in fact the results show the phenyl-*n*-butylethyl system to racemize at a slightly slower rate than the phenyl-*n*-propylethyl system. It would be of interest to investigate the effect of lengthening the chain even further.

The results indicate that racemization occurs almost exclusively via a pyramidal inversion mechanism. Carbon-sulfur bond heterolysis is an unlikely process, formation of methyl, ethyl, *n*-propyl or *n*-butyl carbonium ions being energetically unfavorable. After 10 half-lives of racemization in methanol at 50° only racemic sulfonium

perchlorate salt was isolated, indicating that no decomposition had occurred.

To further examine the effect of introducing bulkier groups into the monoaryldialkyl system, the preparation of the phenyl-t-butylmethyl and phenyl-t-butylethyl systems was attempted. The reaction involved using a mole to mole ratio of phenyl t-butyl sulfide (32) and triethyl or trimethyloxonium fluoroborate, with methylene chloride as solvent. The product of the reaction was a mixture of the desired sulfonium salt, phenyldimethyl or phenyldiethylsulfonium fluoroborate, plus phenyl ethyl or phenyl methyl sulfide. This indicates that the phenyl-t-butylmethyl and phenyl-t-butylethylsulfonium fluoroborate salts are unstable, and readily lose a t-butyl group. Figure XVII outlines a possible scheme. In hydroxylic solvents such as methanol, the phenyl-t-butylmethyl and phenyl-t-butylethyl fluoroborate salts rapidly decomposed yielding phenyl methyl or phenyl ethyl sulfide, t-butyl methyl ether and/or isobutene. The t-butylethylmethylsulfonium system (4) has been found to be stable, hence we can conclude that the steric crowding in the phenyl-t-butylethyl and phenyl-t-butylmethyl systems is so great that ionization to yield a t-butyl carbonium ion and neutral sulfide readily occurs. It may not be simply a question of steric crowding however, since ionization will yield a stable carbonium ion and the neutral sulfide is a good leaving group.

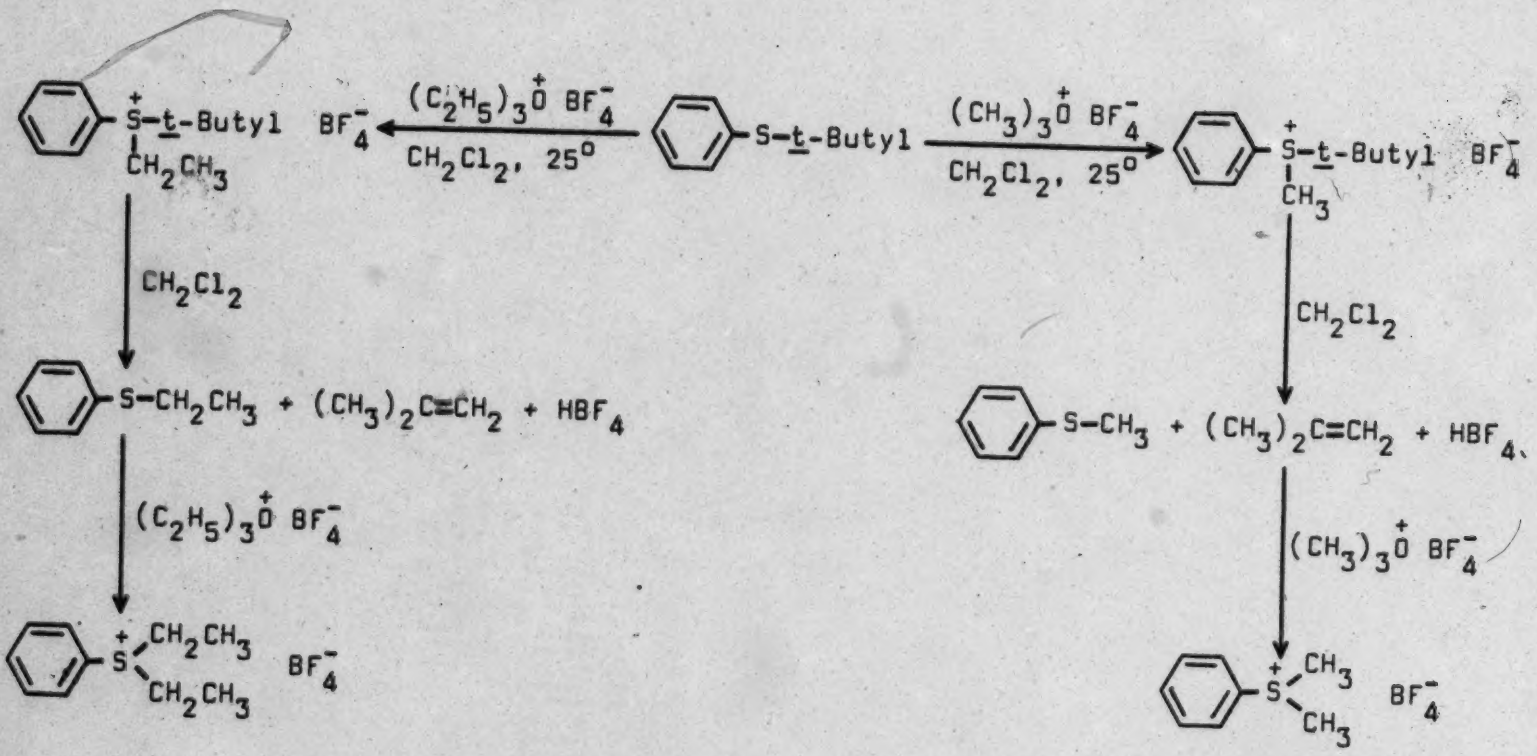
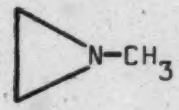


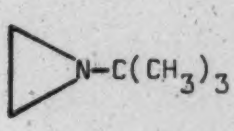
Figure XVII. Attempted preparation and subsequent decomposition of Phenyl-t-butylmethyl and Phenyl-t-butylethylsulfonium fluoroborates.

Steric acceleration of pyramidal inversion has been reported in cyclic systems such as aziridines and oxaziridines (33). Replacement of the $N\text{-}CH_3$ group in compound XII by a $N\text{-}C(CH_3)_3$ group, XIII, leads to ca. 2.5 kcal/mole barrier decrease in the activation energy for inversion.



XII

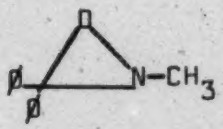
$\Delta H^{\ddagger}$ = 21.3 kcal/mole



XIII

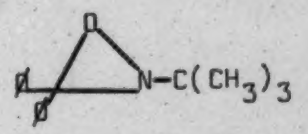
$\Delta H^{\ddagger}$ = 18.6 kcal/mole

If the same structural change is made in the oxaziridine compound XIV to give XV, then the barrier decrease in the activation energy to inversion is greater than 6 kcal/mole.



XIV

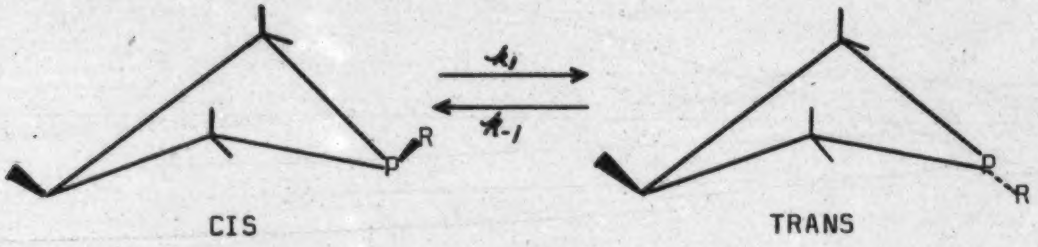
$\Delta H^{\ddagger}$ = 34.1 kcal/mole



XV

$\Delta H^{\ddagger}$ = 27.7 kcal/mole

S. E. Cramer et al (34) have also shown a steric effect to be operative in the inversion of pentamethylphosphetanes.



CIS TRANS

XVI, $R=C_6H_5$ $\rightleftharpoons$ XVII, $R=C_6H_5$ $\Delta H^{\ddagger}$ = 29.8±0.1 kcal/mole

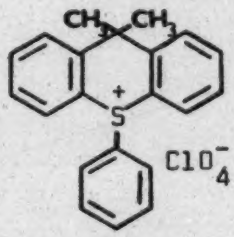
XVIII, R=t-Butyl $\rightleftharpoons$ XIX, R=t-Butyl $\Delta H^{\ddagger}$ = 28.2±0.9 kcal/mole

They conclude from their results that a clear steric affect is operative in the t-butyl derivative, due to the non-bonded interactions with the adjacent methyl groups of the ring. They also point to the possibility of some p-pπ or p-dπ bonding between the phenyl group and the phosphorous in compound XVI. However no evidence is given regarding this possibility.

If all three substituents attached to the sulfur of the sulfonium ion are changed to bulkier groups, a stage may be reached at which steric acceleration will become so great that it would be impossible to isolate the optically active sulfonium salt at room temperature. An attempt to prepare optically active phenyl-o-anisyl-p-tolylsulfonium perchlorate, by the reaction of optically active diarylethoxy sulfonium salts with arylmagnesium halides led to the isolation of racemic triaryl sulfonium salt (35,36). We repeated

Anderson's method, attempting to prepare optically active p-anisyl-p-tolylphenylsulfonium fluoroborate, however, only inactive salt was obtained. Similarly, resolution of the 2R,3R-dibenzoylhydrogentartrate salt proved to be unsuccessful. The results indicate that either the triaryl sulfonium salts were formed via a symmetrical transition state, or else there was a low barrier to the activation energy for inversion. Details of our work are given in the experimental section.

Anderson et al (35) have prepared 9,9-dimethyl-10-phenylthioxanthylium perchlorate, XX, and examined its n.m.r. spectrum at various temperatures.



XX

At room temperature XX has two non-equivalent methyl groups. The n.m.r. signals for the two methyl groups coalesce at 200 ± 5^{o} in solvent benzophenone. From their data, they calculated the free energy of activation, $\Delta G^{\neq}$, for equilibration of the methyl groups as 25.4 kcal/mole. They concluded that non-cyclic triaryl sulfonium salts are in the region of configurational stability where they might or might not show optical activity at room temperature.

Our results can throw some further light on this. Replacement of the ethyl group in the p-anisylphenylethyl

system, XI, by a substituted phenyl group should increase the rate constant for racemization by a factor of *ca.* 10. Using this approximation, the estimated value for the racemization of an optically active triaryl sulfonium salt in methanol at 25° would be 8×10^{-4} sec^{-1}, corresponding to a half-life of *ca.* 15 minutes. This estimate is a minimum value for k_{rac} since it is made on the assumption that steric effects will be mathematically additive in log k_{rac}. It is reasonable to suppose that at some stage steric effects will cease to be additive, and give rise to very large rate accelerations with small structural changes. It seems clear that both Anderson's and our unsuccessful attempts to prepare optically active triaryl sulfonium salts, can be accounted for by rapid racemization of the sulfonium salt during the reaction and isolation procedures. However, it should be pointed out, that given a half-life of 15 minutes and a high specific rotation, then isolation of optically active material should be possible.

TEMPERATURE EFFECTS ON RACEMIZATION

These were calculated as described in Chapter I. The results are shown in Table XXI.

The differences in rate are reflected by changes in the enthalpy and entropy of activation, with the changes in the former being the predominant one. Three estimates to the barrier to inversion of the trimethylsulfonium ion have been made. The energy barriers estimated were 100 kcal/mole (37) and 16-23 kcal/mole (38,39). The former value is much

too high, whereas the latter values are too low. Table XXII presents enthalpy of activation values for several sulfonium salt systems at 50°, showing the variation with increasing steric hindrance around the central sulfur atom. Racemization rate constants and entropies of activation are also shown for comparison.

TABLE XXI

ACTIVATION PARAMETERS FOR THE RACEMIZATION OF THE MONOARYLDIALKYL AND DIARYLMONOALKYLSULFONIUM SYSTEMS IN ANHYDROUS METHANOL AT 50.00°

SYSTEM	$\Delta H^{\ddagger}$ (kcal/mole)	$\Delta S^{\ddagger}$ (e.u.)
p-Anisylphenylmethyl	24.9 ± 0.6	0.7 ± 1.8
p-Anisylphenylethyl	23.9 ± 0.2	1.3 ± 0.8
Phenyl-n-propylethyl	25.4 ± 0.3	2.6 ± 0.9
Phenyl-n-butylethyl	26.1 ± 0.3	4.2 ± 0.9

TABLE XXII

RATE CONSTANTS AND ACTIVATION PARAMETERS FOR PYRAMIDAL INVERSION OF SOME SULFONIUM SALTS AT 50.00°

SYSTEM	SOLVENT	$10^6 k_1$ [a] (sec^{-1})	$\Delta H^{\ddagger}$ (kcal/mole)	$\Delta S^{\ddagger}$ (e.u.)
Phenacylethylmethyl [b]	CH_3OH	1.86	29.2	5
Benzylethylmethyl [b]	CH_3OH	3.48	27.6	2
Phenylethylmethyl	CH_3OH	14.7	27.5	4
1-Adamantylethylmethyl [c]	AcOH	430	26.0	7
Phenyl-n-propylethyl	CH_3OH	161	25.4	3
t-Butylethylmethyl [d]	CH_3CH_2OH	208	25.0	2
p-Anisylphenylmethyl	CH_3OH	148	24.9	1
t-Amylethylmethyl [d]	CH_3CH_2OH	750	24.5	3
p-Anisylphenylethyl	CH_3OH	1020	23.9	1

a) $k_1 = \frac{1}{2}k\alpha$

b) Reference (5)

c) Reference (40)

d) Reference (4)

EXPERIMENTAL

Physical measurements are as described for Chapter I.

para-Anisyl phenyl sulfide

Prepared by the method of Hibert and Johnson (41). After work up a brown oil was obtained, which even after distilling 3X still retained a pale yellow color. Further purification was obtained by use of a Al_2O_3 (Woelm neutral) chromatography column, using 5% diethylether/pentane as solvent.

Yield: 84%. b.p. 142-145° at 4 mm. (reported (41): b.p. 150-152° at 3 mm.). n_D^{20} 1.6253. N.m.r. (neat): τ6.53 (s,3H), 2.51-3.45 (m,9H). Infrared (neat): 560, 1244, 1287, 1492 cm^{-1}.

Anal. Calcd. for $C_{13}H_{12}OS$: C, 72.19; H, 5.59; S, 14.82.
Found: C, 71.99,71.82; H, 5.87, 5.83; S, 15.21, 15.48.

para-Anisylphenylmethylsulfonium fluoroborate

A 2 g. (0.01 mole) quantity of para-anisyl phenyl sulfide was dissolved in 20 ml. of pentane in a round bottomed flask fitted with a drying tube. A 1.5 g. (0.01 mole) quantity of trimethyloxonium fluoroborate was then added. The flask was flushed with nitrogen gas, the drying tube replaced and the mixture magnetically stirred. After allowing the reaction to proceed overnight, a pale yellow oil was obtained. The oil

crystallized as an "off" white solid from methanol/diethylether solution. Further recrystallizations from methanol/diethylether solutions resulted in formation of a white solid.

Yield: 70%. m.p. 52-54.5°. N.m.r. ($CDCl_3$): τ6.42 (s,3H), 6.21 (s,3H), 2.00-3.09 (m,9H). Infrared (nujol): 550, 685, 710, 828, 1050, 1180, 1265, 1448, 1498, 1588, 2860, 2940 cm^{-1}.

<u>para-Anisylphenylmethylsulfonium 2R,3R-dibenzoylhydrogen tartrate</u>

A 6 g. (0.019 mole) quantity of para-anisylphenylmethylsulfonium fluoroborate was dissolved in a minimum quantity of methanol, and passed through a Dowex 1-X8 anion exchange resin in hydroxide ion form. The eluent was neutralized with 7 g. (0.02 mole) of (-)-2R,3R-dibenzoyltartaric acid dissolved in diethylether. The method is the same as that described for the arylethylmethyl systems. After work-up a white solid was obtained.

Yield: 54%. m.p. 144.5-155°. $[\alpha]_D^{25}$ - 78.8° (<u>c</u> 0.3656, anhyd. methanol). N.m.r. (dimethylsulfoxide-<u>d_6</u>): τ6.40 (s,3H), 6.35 (s,3H), 4.48 (s,2H), 2.00-3.35 (m,19H). Infrared (nujol): 548, 705, 1105, 1360, 1445, 1715, 2860, 2930, 2960 cm^{-1}.

The salt was resolved by fractional crystallization from methanol/diethylether solution, as described for the arylethylmethyl systems.

Racemic para-Anisylphenylmethylsulfonium perchlorate

A 3 g. (0.005 mole) quantity of unresolved para-anisylphenylmethylsulfonium 2R,3R-dibenzoylhydrogen tartrate salt, was converted to the perchlorate salt by passage through the anion exchange resin, and neutralization of the eluent with 5% methanolic perchloric acid in the usual way. After work-up a white solid was obtained which was recrystallized 2X from methanol/diethylether solutions.

Yield: 87%. m.p. 53-55°. N.m.r. (dimethylsulfoxide-$\underline{d}_6$): τ6.23 (s,3H), 6.20 (s,3H), 1.80-1.92 (m, 9H). Infrared (nujol): 620, 758, 840, 1090, 1180, 1265, 2940 cm^{-1}.

Anal. Calcd. for $C_{14}H_{12}O_5SCl$: C, 50.83; H, 4.57; S, 9.69.

Found: C, 51.03, 50.72; H, 5.14, 4.81; S, 9.44, 9.37.

(+)-para-Anisylphenylmethylsulfonium perchlorate

A 3.2 g. (0.005 mole) quantity of crystals obtained as the first crop in the resolution of the 2R,3R-dibenzoylhydrogen tartrate salt was converted to the perchlorate as described for the racemic material. However, the eluent was collected in a flask immersed in an ice/salt bath to minimize any racemization. After work-up an oil was obtained which solidified on cooling to 5°. The resulting white solid was recrystallized 2X from methanol/diethylether solutions.

Yield: 88%. m.p. 56.5-59.5°. $[\alpha]_{365}^{25}$ + 21.2° ($\underline{c}$ 0.9790, anhyd. methanol). N.m.r. ($CDCl_3$): τ6.40 (s,3H), 6.21 (s,3H), 1.94-3.09 (m,9H). Infrared (nujol): 693, 743, 832,

1070, 1248, 1493, 1590, 3430 cm^{-1}.

Anal. Calcd. for $C_{14}H_{12}O_5Cl$: C, 50.83; H, 4.57; S, 9.96.

Found: C, 50.58, 50.88; H, 4.38, 4.52; S, 9.43, 9.55.

(-)-para-Anisylphenylmethylsulfonium perchlorate

A 4.7 g. (0.008 mole) quantity of crystals obtained from the mother liquor in the resolution of the 2R,3R-dibenzoylhydrogen tartrate salt was converted to the perchlorate salt as described for the (+)-isomer. After work-up an oil was obtained, which after being kept at 5° for several days, yielded a "pasty" solid. The material was recrystallized from methanol/diethylether solutions, however it still retained its "pasty" nature.

m.p. 47-50°. $[\alpha]_{365}^{25}$ - 15.2° (c 1.172, anhyd. methanol).

N.m.r. ($CDCl_3$): τ6.37 (s,3H), 6.20 (s,3H), 1.81-3.13 (m,9H).

Infrared (nujol): 620, 758, 840, 1090, 1180, 1256, 2940 cm^{-1}.

No analysis done.

para-Anisylphenylethylsulfonium fluoroborate

A 5 g. (0.023 mole) quantity of para-anisyl phenyl sulfide was dissolved in methylene chloride. A 4.1 g. (0.023 mole) quantity of triethyloxonium fluoroborate was added, the flask flushed with nitrogen gas, and then fitted with a drying tube. The mixture was stirred magnetically and left overnight. After work-up, the initially formed oil yielded a white solid when crystallized from acetone/diethylether solution.

Yield: 90%. m.p. 53-55°. N.m.r. (dimethylsulfoxide-$\underline{d}_6$): τ8.69 (t,3H,J=7.5 c.p.s.), 6.07 (s,3H), 5.33-5.88 (q,2H), 1.67-2.83 (m,9H). Although adjacent to an assymetric centre, no splitting was observed in the quartet. Infrared (KBr): 693, 743, 832, 1070, 1248, 1493, 1590, 3430 cm^{-1}.

<u>para-Anisylphenylethylsulfonium 2R,3R-dibenzoylhydrogen tartrate</u>

A 2 g. (0.006 mole) quantity of para-anisylphenylethylsulfonium fluoroborate was dissolved in a minimum amount of methanol, and converted to the 2R,3R-dibenzoylhydrogen tartrate salt by passage through the anion exchange resin and neutralization of the eluent with (-)-2R,3R-dibenzoyl tartaric acid in the usual way. After work-up a white solid was obtained.

Yield: 80%. m.p. 119-121°. $[\alpha]_D^{25}$ - 73.3° ($\underline{c}$ 0.4736 anhyd. methanol). N.m.r. (acetic acid-$\underline{d}_4$): τ9.06 (t,3H,J=7.5 c.p.s.), 6.59 (s,3H), 6.11-6.50 (q,2H), 4.28 (s,2H), 2.16-3.42 (m,19H). Infrared (KBr): 712, 1118, 1268, 1590, 1718 cm^{-1}.

The salt was resolved by fractional crystallization from methanol/diethylether solution as described for the arylethylmethyl systems. The salt however, is only sparingly soluble in methanol (i.e., 2.5 g. dissolved in 150 ml.).

<u>Racemic para-Anisylphenylethylsulfonium perchlorate</u>

A 5 g. (0.015 mole) quantity of para-anisylphenylethylsulfonium fluoroborate was dissolved in a minimum

amount of methanol and converted to the perchlorate salt in the usual way. After work-up the initially formed oil soon solidified on cooling to 5°. The salt was recrystallized 3X from methanol/diethylether solutions.

Yield: 90%. m.p. 72-73.5°. N.m.r. (dimethylsulfoxide-$\underline{d}_6$): τ8.79 (t,3H,J=7.5 c.p.s.), 6.25 (s,3H), 5.57-6.03 (q,2H), 1.86-3.02 (m,9H). Infrared (KBr): 1110, 1120, 1248, 1495, 1593, 1630, ca. 3440 cm^{-1}.

Anal. Calcd. for $C_{15}H_{17}O_5SCl$: C, 52.25; H, 4.97; S, 9.30.
Found: C, 52.19, 51.84; H, 4.71, 4.75; S, 9.35, 9.05.

(+)-para-Anisylphenylethylsulfonium perchlorate

A 2 g. (0.003 mole) quantity of the first crop of crystals obtained in the resolution of the 2R,3R-dibenzoyl-hydrogen tartrate salt was converted to the optically active perchlorate salt in the usual way. The eluent was allowed to drip into a flask immersed in an ice/salt bath to minimize any racemization. After work-up, the white solid was recrystalized from methanol/diethylether solution. The salt was stored at -10° overnight and the racemization rates run the following day.

Yield: 85%. m.p. 39-40°. N.m.r. (dimethylsulfoxide-$\underline{d}_6$): τ8.84 (t,3H,J=7.5 c.p.s.), 6.32 (s,3H), 5.49-6.15 (q,2H), 1.70-3.19 (m,9H). Infrared (KBr): 625, 685, 748, 832, 1090, 1182, 1270, 1305, 1448, 1500, 1590, 3420 cm^{-1}.

Anal. Calcd. for $C_{15}H_{17}O_5SCl$: C, 52.25; H, 4.97; S, 9.30.
Found: C, 52.37, 52.11; H, 4.82, 5.27; S, 9.49, 9.25.

No rotation was done because of the rapid loss of optical activity of the salt at room temperature (25°).

(-)-para-Anisylphenylethylsulfonium perchlorate

A 2 g. (0.003 mole) quantity of the crystals from the mother liquor in the resolution of the 2R,3R-dibenzoyl-hydrogen tartrate salt, was converted to the optically active perchlorate as described for the (+)-isomer.

Yield: 90%. m.p. 64-68.5°. N.m.r. (dimethylsulfoxide-$\underline{d}_6$): τ8.84 (t,3H,J=7.5 c.p.s.), 6.33 (s,3H), 5.63-6.11 (q,2H), 1.92-3.10 (m,9H). Infrared (KBr): superimposable with (+)-isomer.

Anal. Calcd. for $C_{15}H_{17}O_5SCl$: C, 52.25; H, 4.97; S, 9.30.
Found: C, 52.39, 52.07; H, 4.72, 5.03; S, 9.16, 9.15.

Again, no rotation is recorded because of the rapid loss of optical activity at room temperature (25°).

Phenyl n-butyl sulfide

Prepared as described by V. P. Ipatieff, Herman Pines and B. S. Friedman (32).

Yield: 90%. b.p. 101-102° at 9 mm. (reported (32): 94.5-97.0° at 4 mm.). n_D^{25} 1.5460 (reported (32): n_D^{20} 1.5463). N.m.r. (neat): τ8.50-9.71 (m,7H), 7.53 (t,2H), 2.83-3.42 (m,5H). Infrared (neat): 690, 738, 1025, 1438, 1480, 1583, 2870, 2930, 2960 cm^{-1}.

Phenyl-n-butylethylsulfonium fluoroborate

A 10 g. (0.06 mole) quantity of phenyl n-butyl

sulfide was dissolved in 25 ml. of methylene chloride in a flask fitted with a drying tube. The flask was flushed with nitrogen gas, and 11.5 g. (0.06 mole) of triethyloxonium fluoroborate added. The drying tube was replaced and the mixture stirred magnetically. The reaction was complete in about an hour, addition of diethylether resulted in formation of an oil which soon solidified on cooling to 5°. The white solid was filtered and recrystallized 2X from methanol/diethylether solutions.

Yield: 95%. m.p. 35-36°. N.m.r. ($CDCl_3$): τ8.00-9.23 (m,10H), 5.83-6.42 (m,4H), 1.72-2.33 (m,5H). Infrared (KBr): 1085, 1124, 1630, 3430 cm^{-1}.

Phenyl-n-butylethylsulfonium 2R,3R-dibenzoylhydrogen tartrate

A 5 g. (0.018 mole) quantity of phenyl-n-butylethylsulfonium fluoroborate was dissolved in a minimum amount of methanol and converted to the 2R,3R-dibenzoylhydrogen tartrate salt in the usual manner. After work-up, a white solid was obtained.

Yield: 90%. m.p. 115.5-117.5°. $[\alpha]_D^{25}$ - 82.0° (c 0.4100, anhyd. methanol). N.m.r. (dimethylsulfoxide-d_6): τ8.42-9.68 (m), 5.68-7.42 (m), 4.29 (s), 1.84-3.00 (m). Infrared (KBr): 718, 1105, 1265, 1625, 1708, 3420 cm^{-1}.

The salt was resolved by fractional crystallization from methanol/diethylether solution, as described for the arylethylmethyl systems.

Racemic Phenyl-n-butylethylsulfonium perchlorate

A 5 g. (0.018 mole) quantity of phenyl-n-butylethylsulfonium fluoroborate was dissolved in a minimum quantity of methanol, passed through the anion exchange resin, and converted to the perchlorate salt in the usual manner. After work-up a white solid was obtained which was recrystallized 2X from methanol/diethylether solutions.

Yield: 90%. m.p. 45-47°. N.m.r. ($CDCl_3$): τ8.03-9.29 (m,10H), 5.06-6.36 (m,4H), 1.71-2.32 (m,5H). Infrared (KBr): 625, 760, ca. 1090, 1448, 3420 cm^{-1}.

Anal. Calcd. for $C_{12}H_{19}O_4SCl$: C, 48.89; H, 6.50; S, 10.88.
Found: C,48.88, 49.34; H, 6.30, 6.32; S, 10.83, 10.82.

(-)-Phenyl-n-butylethylsulfonium perchlorate

A 3 g. (0.005 mole) quantity of the first crop of crystals obtained in the resolution of the 2R,3R-dibenzoylhydrogen tartrate salt was dissolved in a minimum quantity of methanol and converted to the optically active perchlorate salt in the usual manner. The eluent was collected in a flask immersed in an ice/salt bath to minimize any racemization. After work-up a white solid was obtained which was recrystallized 2X from methanol/diethylether solutions.

Yield: 90%. m.p. 32.5-34.0°. $[\alpha]_{365}^{25}$ - 10.8° (c 1.129, anhyd. methanol). N.m.r. ($CDCl_3$): τ8.09-9.32 (m,10H), 5.83-6.34 (m,4H), 1.73-2.31 (m,5H). Infrared (KBr): 625, 760, ca. 1090, 1448, 3420 cm^{-1}.

Anal. Calcd. for $C_{12}H_{19}O_4SCl$: C, 48.89; H, 6.50; S, 10.88.

Found: C, 49.21, 48.79; H, 6.33, 6.56; S, 10.38, 10.99.

Phenyl n-propyl sulfide

Prepared as described by Ipatieff et al (32).

Yield: 90%. b.p. 200-205° at 700 mm. (reported (32): 218.5-219.5° at 750 mm.). n_D^{20} 1.5568 (reported (32): n_D^{20} 1.5571). N.m.r. (neat): τ9.21-9.62 (m,3H), 8.39-9.09 (m,2H), 7.58 (t,2H), 2.88-3.38 (m,5H). Infrared (neat): 690, 739, 1024, 1440, 1480, 1585, 2970 cm^{-1}.

Phenyl-n-propylethylsulfonium fluoroborate

A 5.85 g. (0.04 mole) quantity of phenyl n-propyl sulfide was dissolved in 25 ml. of methylene chloride. A 7.3 g. (0.04 mole) quantity of triethyloxonium fluoroborate was then added, the flask flushed with nitrogen gas and fitted with a drying tube. The mixture was magnetically stirred for one hour, addition of diethylether resulted in precipitation of a white solid. The salt was recrystallized 2X from methanol/diethylether solutions.

Yield: 88%. m.p. 55-56°. N.m.r. ($CDCl_3$): τ7.99-9,09 (m,8H), 5.93-6.43 (m,4H), 1.76-2.36 (m,5H). Infrared (KBr): 685, 709, 1080, 1118, 1440, 1625, 3430 cm^{-1}.

Phenyl-n-propylethylsulfonium 2R,3R-dibenzoylhydrogen tartrate

A 6 g. (0.023 mole) quantity of phenyl-n-propyl-ethylsulfonium fluoroborate was converted to the 2R,3R-dibenzoylhydrogen tartrate salt in the usual manner. After

work-up a white solid was obtained.

Yield: 90%. m.p. 100-105°. $[\alpha]_D^{25}$ - 79.9° (c 0.4804, anhyd. methanol). N.m.r. (dimethylsulfoxide-d_6): τ8.42-9.54 (m,8H), 6.06-6.98 (m,4H), 4.38 (s,2H), 1.83-3.00 (m,15H). Infrared (KBr): 715, 1110, 1262, 1449, 1627, 1715, 3430 cm^{-1}.

The salt was resolved by fractional crystallization from methanol/diethylether solution, as described for the aryl-ethylmethyl sulfonium systems.

Racemic Phenyl-n-propylethylsulfonium perchlorate

A 5 g. (0.02 mole) quantity of phenyl-n-propyl-ethylsulfonium fluoroborate was dissolved in a minimum amount of methanol, and converted to the perchlorate salt in the usual way.

Yield: 90%. m.p. 60.0-62.5°. N.m.r. ($CDCl_3$): τ7.93-9.16 (m,8H), 5.96-6.43 (m,4H), 1.84-2.42 (m,5H). Infrared (KBr): 620, 630, 682, 750, 1090, 1440, 3420 cm^{-1}.

Anal. Calcd. for $C_{11}H_{17}O_4SCl$: C, 47.06; H, 6.10; S, 11.42.

Found: C, 47.38, 46.90; H, 6.06, 5.84; S, 11.30, 11.45.

(+)-Phenyl-n-propylethylsulfonium perchlorate

A 3.2 g. (0.006 mole) quantity of the first crop of crystals obtained in the resolution of the 2R,3R-dibenz-oylhydrogen tartrate salt was dissolved in a minimum amount of methanol, and converted to the optically active perchlor-ate salt in the usual way. The eluent was collected in a flask immersed in an ice/salt bath to minimize any racemiza-

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tion. After work-up, a white solid was obtained which was recrystallized 2X from methanol/diethylether solutions.

Yield: 85%. m.p. 42-47°. $[\alpha]^{25}_{365}$ + 41.3° (c 1.030, anhyd. methanol). N.m.r. ($CDCl_3$): τ7.99-9.16 (m,8H), 5.90-6.53 (m,4H), 1.82-2.49 (m,5H). Infrared (KBr): 620, 630, 682, 750, 1090, 1440, 3420 cm^{-1}.

Anal. Calcd. for $C_{11}H_{17}O_4SCl$: C, 47.06; H, 6.10; S, 11.42.
Found: C, 47.24, 47.12; H, 5.98, 5.68; S, 11.42, 11.46.

(-)-Phenyl-n-propylethylsulfonium perchlorate

A 3 g. (0.005 mole) quantity of the crystals obtained from the mother liquor in the resolution of the 2R,3R-dibenzoylhydrogen tartrate salt, was converted to the optically active perchlorate as described for the (+)-isomer. After work-up the white solid was recrystallized 2X from methanol/diethylether solutions.

Yield: 85%. m.p. 50-54°. $[\alpha]^{25}_{365}$ - 19.7° (c 1.108, anhyd. methanol). N.m.r. ($CDCl_3$): τ7.98-9.19 (m,8H), 5.91-6.57 (m,4H), 1.76-2.49 (m,5H). Infrared (KBr): superimposable with (+)-isomer.

Anal. Calcd. for $C_{11}H_{17}O_4SCl$: C, 47.06; H, 6.10; S, 11.42.
Found: C, 46.87, 47.41; H, 6.07, 6.28; S, 11.28, 11.45.

TRIARYL SULFONIUM SALTS

Anderson et al (35) have prepared several triaryl sulfonium salts, however, their attempts to prepare the salts

in optically active form were unsuccessful. We repeated Anderson's work, although at the time we lacked his precise experimental details, consequently, our method differs somewhat from theirs.

(+)-para-Tolyl phenyl sulfide

Prepared as described by Anderson et al (42). Yield: 90%. m.p. 91-92° (reported (42): 92-93°). $[\alpha]_D^{25}$ + 20.0° (c 0.9040, acetone) (reported (42): +22.0° (c 2.00, acetone)). N.m.r. ($CDCl_3$): τ7.74 (s,3H), 2.21-2.93 (m,9H). Infrared (nujol): 1378, 1460, 2920 cm^{-1}.

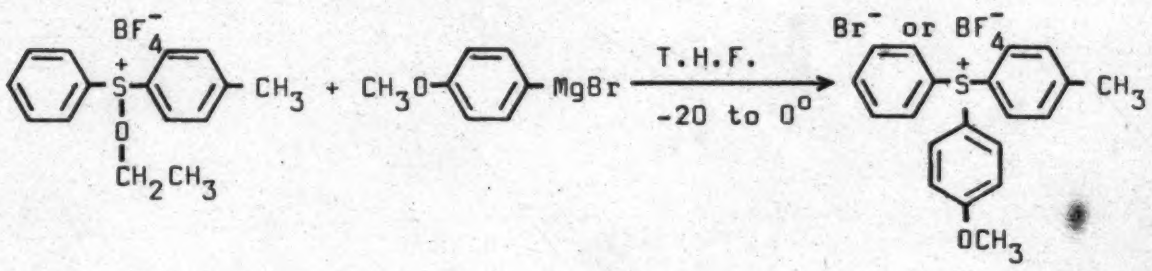
(+)-para-Tolylphenylethoxysulfonium fluoroborate

Prepared as described by C. R. Johnson and D. McCants (43). After work-up an oil was obtained, all attempts to obtain a crystalline material were unsuccessful.

Yield: 100%. $[\alpha]_D^{25}$ + 27.6° (c 0.5690, methylene chloride). N.m.r. ($CDCl_3$): τ8.52 (t,3H,J=7.0 c.p.s.), 7.58 (s,3H), 5.20-5.63 (q,2H), 1.95-2.67 (m,9H). Infrared (neat): 760, 880, 1065, 1442, 1595, 2980 cm^{-1}.

Note: The solution used for the specific rotation measurement was left overnight in the polarimetric tube. A measurement taken the following day showed no change in rotation, indicating that the ethoxy sulfonium salt is optically stable at 25°.

Attempted preparation of optically active para-Tolyl-para-anisylphenylsulfonium salt



The Grignard was prepared from 2.08 g. (0.015 mole) of p-bromoanisole and 0.58 g. (0.025 g-atom) of Mg, using purified tetrahydrofuran (44) as solvent. This was added over a one hour period to a 2.5 g. (0.0075 mole) quantity of the optically active ethoxy sulfonium salt dissolved in 15 ml. of purified tetrahydrofuran. The temperature was kept at about -10° by means of a methanol/ice bath. After the addition was complete, the mixture was stirred a further hour. The mixture was then hydrolyzed with a cooled saturated solution of ammonium chloride and the aqueous layer extracted 3X with cooled chloroform. Addition of diethylether resulted in formation of a pale yellow oil. A rotation measurement, using methanol as solvent, was carried out immediately. The material was found to be optically inactive.

Yield: ca. 50%. N.m.r. ($CDCl_3$): τ7.59 (s,3H), 6.16 (s,3H), 2.13-2.93 (m,13H). Infrared (neat): 673, 692, 818, 842, 1050, 1185, 1250, 1275, 1320, 1452, 1500, 1594, 2960, 3040 cm^{-1}.

The peak at 1050 cm^{-1} indicates the presence of the fluoroborate anion, suggesting that the reaction produces at least some triaryl sulfonium fluoroborate. The presence of some sulfonium bromide cannot, however, be discounted.

Note: The method outlined above differs from Anderson's preparation of p-tolyl-m-anisylphenyl and p-tolyl-m-tolylphenylsulfonium salts in several respects. After preparation of his ethoxy sulfonium salts (p-tolyl-m-anisyl and p-tolyl-m-tolylethoxysulfonium fluoroborate), he replaced the methylene chloride solvent with 1,2-dimethoxyethane. His Grignard (phenylmagnesium bromide) was prepared in diethylether and then added over a 30 minute period to the ethoxy sulfonium salt solution kept at -20 to -10°. After addition was complete, the mixture was immediately hydrolyzed with saturated ammonium chloride solution. The aqueous layer was extracted several times with chloroform, the solution concentrated, and the salt precipitated out by the addition of diethylether. He reports a 36% yield at this point. The salt was then dissolved in distilled water, acidified, and precipitated out as the perchlorate salt by the addition of aqueous sodium perchlorate solution at 0°. Optical rotation measurements were then performed on the perchlorate salts.

Conclusions:

Formation of optically inactive products could be explained in several ways. Firstly, the ethoxy sulfonium salt might racemize before it reacts with the Grignard to form products. However, if these salts do racemize then they

must do so in the Grignard solution, since otherwise they are optically stable. Secondly, the reaction might proceed through a symmetric intermediate or transition state. This seems unlikely when one considers other examples of nucleophilic substitution at sulfur involving optically active tri-coordinate sulfur (equations (i) and (ii)), which proceed with inversion to give optically active products.

$$ArS(O)OR + RMgX \longrightarrow ArRSO \quad (i) \quad (45)$$

$$ArAr^1\overset{+}{S}OC_2H_5 + OH^- \longrightarrow ArAr^1SO \quad (ii) \quad (43)$$

To test this hypothesis we attempted to prepare optically active diarylalkylsulfonium salts by treatment of the optically active diarylethoxysulfonium salt with alkylmagnesium halides. Formation of optically inactive product would indicate a symmetric intermediate or transition state, since we have already prepared diarylalkylsulfonium salts in optically active form. However the product of the reaction was the sulfoxide, none of the desired material could be detected.

A third possibility is racemization via aryl group exchange with the arylmagnesium halide. However, Anderson et al (35) have shown this process to be non-operative in the reaction. We are thus left with the possibility that racemization occurs after the formation of the triaryl sulfonium salt via a pyramidal inversion mechanism, optical activity being lost in the work-up and isolation procedures.

In our case this amounted to approximately 45-60 minutes. Using our estimate of the racemization rate at 25° for the triaryl system, and given a low specific rotation for the salt, then failure to observe any optical activity is not so surprising.

para-Tolyl-para-anisylphenylsulfonium 2R,3R-dibenzoyl-hydrogen tartrate

A 2 g. quantity of the presumed fluoroborate salt was dissolved in methanol and passed through a Dowex 1-X8 anion exchange resin in hydroxide ion form. The eluent was neutralized with a diethylether solution of (-)-2R,3R-dibenzoyl tartaric acid. After work-up the initially formed oil yielded a white solid when crystallized from acetone/diethylether solution.

m.p. *ca.* 50-65° (turned glassy). $[\alpha]_D^{25}$ - 49.3° (*c* 1.084, anhyd. methanol). N.m.r. ($CDCl_3$): τ7.78 (s,3H), 6.34 (s,3H), 3.91 (s,2H), 1.84-3.18 (m,23H). Impurity peaks occurred at τ8.83 and 4.58. Infrared (nujol): 770, 1025, 1068, 1265, 1375, 1460, 1710, 2850, 2920 cm^{-1}.

Attempted resolution via fractional crystallization from acetone/diethylether solution gave no good evidence for separation of the diastereoisomers. However, it is noteworthy that rotation measurements taken immediately on the first 2R,3R-dibenzoylhydrogen tartrate salt formed in an attempted separation (in this particular case, an oil), did show changes in rotation with time. More work is needed

to verify this observation.

KINETICS

Titrimetric rates

The sealed ampoule method was used as described in Chapter I.

Racemization rates

Both Method I and Method II as described in Chapter I were employed.

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ADDITION/OMISSION

Preparation of (+)-Phenyl-n-butylethylsulfonium perchlorate

A 4 g. (0.007 mole) quantity of the crystals obtained from the mother liquor in the resolution of the 2R,3R-dibenzoylhydrogen tartrate salt was converted to the optically active perchlorate salt as described for the (-)-isomer. After work-up the white solid was recrystallized from methanol/diethylether solutions.

Yield: 80%. m.p. 37.5-39.0°. $[\alpha]_{365}^{25}$ + 24.0° (c 1.203, anhyd. methanol). N.m.r. ($CDCl_3$): τ8.02-9.33 (m,10H), 5.84-6.36 (m,4H), 1.72-2.33 (m,5H). Infrared (KBr): superimposable with (-)-isomer.

Anal. Calcd. for $C_{12}H_{19}O_4SCl$: C,48.89; H, 6.50; S, 10.88.
Found: C, 49.25, 48.86; H, 6.55, 6.28; S, 10.95, 10.81.

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